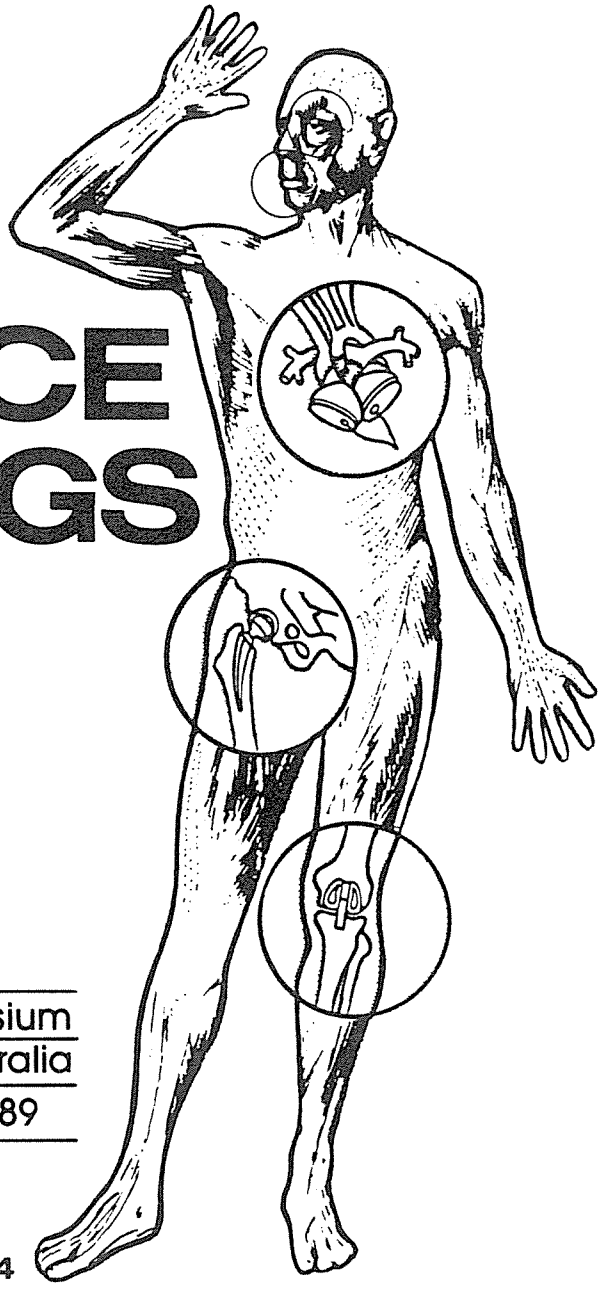
Royal Australian Chemical Institute
Western Australian Polymer Group

and

Australian Foundation for Prevention of
Blindness — Lions Eye Institute

ADVANCES IN BIOMEDICAL POLYMERS

CONFERENCE PROCEEDINGS



International Symposium
Perth — Western Australia
5th-9th February 1989

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I N D E X

GENERAL ANNOUNCEMENTS

The organizing committee reserves the right to alter the programme. All programme changes will be displayed on the noticeboards adjacent to the registration desk. PLEASE CHECK THE NOTICEBOARDS.

Authors should check the starting time/s for their paper/s. The programme is made up from 20 minute slots. Contributed papers have been allocated one slot, invited papers two slots and plenary papers three slots. The time slots include introduction and question time. For example a 20 minute slot should allow authors 15 minutes paper presentation time.

Authors of paper presentations are requested to attend the lecture theatre 15 minutes before the commencement of the session in which their paper is to be presented. This is to make sure the projectionist has

slides etc. set up in accordance with the speakers wishes and for the session Chairman to issue any last minute instructions.

Papers will start and finish promptly at the advertised times. Posters will be displayed for the duration of the conference. Poster authors are requested to attend their posters during the advertised poster session times.

To gain entry to Workshop and Symposium lectures and other functions ALL delegates are requested to wear the name badges issued at registration.

INTRODUCTION:

The challenge was invited about three years ago by Lions Eye Institute for the W.A.Polymer Group RACI to organize an international symposium on biomaterials. The state Polymer Group was then only in its infancy. We didn't have one committee member with biomaterials experience to guide us. The task seemed daunting but initial indications of support were encouraging. Prof. Ian Constable, Director, Lions Eye Institute offered to underwrite such a conference and the challenge was accepted.

During the lead time we seconded a number of people from other professions related to the conference topic areas. Their input was invaluable. A great deal of appreciation is extended to Dr. Traian Chirila of Lions Eye Institute and Mr. Ed Scull from Department of Bioengineering at Royal Perth Hospital without whose help the committee would have been struggling.

At times over the past three years I have often wondered how a specialist in historical buildings restoration could become involved in a biomaterials conference. Each time I reflected I realised that the restoration of old buildings isn't significantly different to restoration of human bodies. Both demand skill, care and a good knowledge of modern materials together with an innovative approach.

The progresses in fundamental polymer science are usually far in advance of the applications of materials to real life situations. The adaptability of new materials to medicine usually requires manipulation of current technology to specific application. This means, of course, that polymer science maintains a high profile at the interface of technology and society.

Society continues to demand greater extension to the quality and quantity of life. This places enormous demands on medicine and science in general. In the past two decades medical science has made great in-roads in the replacement of natural body parts to

prolong life. However, demand always exceeds supply and use of synthetic materials as natural substitutes will be with us well into the future.

The innovative adaption of existing thermoplastics and thermosets including polyethylene, polymethylmethacrylate, polyurethane, epoxies and composite materials for medical use leads the polymer scientist into the realms of the biological sciences. A multidisciplinary approach to the understanding of polymer/physiological interactions is the only way the use of synthetic biomaterials can advance. It is for this reason that the multidisciplinary emphasis for this conference was taken.

The organizing committee extends a warm welcome to all delegates and speakers and hopes their visit to Perth is especially enjoyable and rewarding. To the sponsors and exhibitors who have also contributed to the production of this symposium the committee also extends their appreciation.

Grant M. Ferguson
Chairman
W. A. Polymer Group RACI

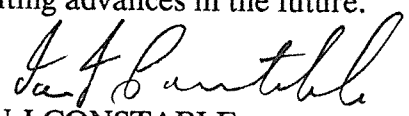
FOREWORD

THE BIOMEDICAL POLYMER CHALLENGE

As scientists, engineers, surgeons and physicians probe ever deeper into the material and biological interface, major advances in the restoration of human function continued to evolve. Nature, in the course of millions of years of evolution, has evolved a magnificent functioning human apparatus of extraordinary complexity, adaptability and finesse. So good is this product of evolution that man himself is increasingly able to design, develop and use biomaterials to replace his own parts with materials that function almost as well as the real thing. It is truly remarkable that, at least in this sense, man is natures product and in turn is helping nature to repair itself.

This congress has attracted a large number of acknowledged world experts to a relatively isolated but intellectually vibrant part of the earth to discuss biomedical polymers, their scientific characteristics, development as useful biomaterials and their particular applications in ophthalmology, dentistry, cardio-vascular surgery and orthopaedics. So useful have biomaterials become in many fields of medicine that a whole day's symposium will be devoted to bio-compatibility and bio-degradation. In each of the surgical speciality areas the inventiveness of biochemists, biophysicists and bioengineers and their collaboration with surgeons, have spawned extensive scientific disciplines in their own right, as well as multi-million dollar industries. In a relatively short space of time, contact lenses, intra-ocular lenses, heart valves, artificial blood vessels, dental prosthetic materials and orthopaedic prostheses have become routine fundamental components of these vast surgical specialities. Yet, no biomaterials can be deemed to be perfect and many problems await the inventiveness and ingenuity of multi-disciplinary research and development teams.

This truly international symposium will delineate many new advances and highlight problems still to be solved. The fact that experts from so many countries and so many disciplines have assembled to exchange information at the leading edge of biopolymer science, assures the success of this meeting and promises even more exciting advances in the future.



IAN J CONSTABLE
Director - Lions Eye Institute
Secretary - Australian Foundation
for Prevention of Blindness WA Inc

11 January 1989

ADVANCES IN BIOMEDICAL POLYMERS SYMPOSIUM

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SYMPOSIUM PROGRAMME

MONDAY 6 FEBRUARY, 1989.
8.30am Registration

SESSION 1. OPENING
9.00am Introduction - Grant M.Ferguson - Chairman, RACI W.A.Polymer Group.

9.15am Opening speech - Prof. Ian Constable - Director, Lions Eye Institute.

9.45am Morning Tea

Chairman - Ian Constable

SESSION 2. POLYMERS IN OPHTHALMOLOGY
10.15am Plenary Lecture -
Prof. B.J. Tighe (University of Aston in Burmingham, UK) - **"Hydrogels at Biological Interfaces"**

11.15am -
J.Rechberger, T. Grant and D. Sweeney (CCLRU, University of NSW, Aust.) - **"Efficiency of Protein Removal for Soft Contact Lenses".**

11.35am -
Graham D.Barrett (Lions Eye Institute, Perth, W.Aust.) **-"Hydrogels as Biomaterials for Intraocular Lens Implants".**

11.55am - Lunch

Chairman - David Cock

SESSION 3. POLYMERS IN DENTISTRY
1.10pm Plenary Lecture -
Dr. H.Oysaed (NIOM - Scandinavian Inst. of Dental Materials, Norway) - **"Characterization of Multiphase Methacrylate Based Polymers and Composites for Dental Application".**

2.10pm -
M.Letort and M.F.Sigot-Luizard (Universite de Compiegne, France) - **"In Vitro Cytocompatibility Assessment of Biomaterials Toward Gingival Tissue by Organ Culture Method: Application to Different Dental Materials".**

2.30pm -
P.J.Mack (UWA Dental School, W.Aust.) - **"Dental Soft Lining Polymers".**

2.50pm - Afternoon Tea

Chairman - Peter Mack

SESSION 4. POLYMERS IN DENTISTRY
3.20pm Invited Lecture -
Dr. M.J. Tyas (Australian Dental Standards Laboratory, Melbourne, Aust.)- **"Clinical Use of Composite Resins in Dentistry".**

4.05pm -
K. Ekstrand and I.E.Ruyter (NIOM, Oslo, Norway) - **"Carbon/Graphite Fibre Reinforced Polymethylmethacrylate for Implant-Fixed Dental Bridges.**

4.25pm Invited Lecture -
Dr. W.D. Cook (Medical Devices and Dental Products Branch, Melbourne, Aust.) - **"Dental Restorative Materials - Structure and Properties".**

5.05pm End Session 4

7.00 - 9.30 Poster Session

TUESDAY 7 FEBRUARY, 1989.

Chairman - Dave Hill

SESSION 5. POLYMERS IN CARDIOVASCULAR SURGERY
9.00am Plenary Lecture -
Prof. Stuart L.Cooper (Dept. Chem. Eng., U.Wisconsin, USA) - **Protein Adsorption on Polyurethane Biomaterials - the role of vitronectin in blood-surface interactions.**

10.00am - Morning Tea

Chairman - Wayne Cook

SESSION 6. POLYMERS IN CARDIOVASCULAR SURGERY
10.30am Invited lecture -
Dr. H.D. Wagner (Dept. Materials Research, Weizmann Institute of Science, Israel) - **"Failure of Vascular Grafts: Correlation with Structure and Material Properties".**

11.10am -
K. Kottke-Marchant, J.M. Anderson, Y. Umenura and R.E. Marchant (Dept. Macromol. Science and Pathology, Case Western Reserve University, Ohio, USA) - **"The Effect of Albumin on the In Vitro Blood Compatibility of Dacron Arterial Prosthesis".**

11.30am -
Dr. Chris C.Berndt, D. Collinson, G.Edwards and G.Roberts (Monash University and Bio Nova Neo Technics Pty. Ltd., Melbourne, Aust.) - **"The Tensile Properties of Vascular Prostheses".**

11.50am -
M.J. Slepian and A Schindler (Research Triangle Institute, Research Triangle Park, Ohio, USA) - **"Polymeric Endolumina' Paving/Sealing: A Biodegradabable Alternative to Intravascular Stenting".**

12.10 - Lunch

Chairman - Ed Scull

SESSION 7. POLYMERS IN ORTHOPAEDICS
1.15pm Plenary Lecture -
Prof. G.W.Hastings (North Staffordshire Polytechnic, UK) - **"Polymer Composites for Orthopaedic Implants"**

2.15pm Invited Lecture -
Dr. S.H.Teoh (National University of Singapore) - **"Selection of Polymeric Materials for Cosmetic Hand Prosthesis".**

2.35pm
A.P.Skirving and R.Day (Royal Perth Hospital, Perth, W.A.,Aust.), **"Clinical and Experimental Comparison of Carbon Fibre Plates versus Stainless Steel Dynamic Compression Plates in the Treatment of Fractures".**

2.55pm - Afternoon Tea

Chairman - Traian Chirila

SESSION 8. POLYMERS IN OPHTHALMOLOGY

3.30Pm Invited Lecture -
Prof. N.A. Peppas (School of Chemical Engineering, Purdue University, USA) - **"Diffusive and Surface Problems During Utilization of Hydrogels in Ophthalmology".**

3.50pm FUTURE DIRECTIONS DISCUSSION
Chairman: Dr. Wayne Cook (Medical Devices and Dental Standards Branch Commonwealth Dept. of Health, Melbourne, Aust.)
Panel: Dr. A. Jones (Department of Industry, Technology and Commerce [DITAC], Aust.)
Prof. R.E.Marchant (Case Western Reserve University, USA)

Dr. C.C. Berndt (Monash University, Aust.)
Prof. B.J. Tighe (University of Aston in Burmingham, UK)
Prof. G.W. Hastings (North Staffordshire Polytechnic, UK)
Prof. P.C. Farrell (University of N.S.W., Aust.)
Dr. H.D. Wagner (Weizmann Institute of Science, Israel)
Prof. N.A. Peppas (Purdue University, USA)
Dr. H. Oysaed (NIOM, Scandinavian Institute of Dental Materials, Norway)

5.05pm End Day 2

WEDNESDAY 8 FEBRUARY, 1989.

Chairman - Traian Chirila

SESSION 9. POLYMERS IN OPHTHALMOLOGY
9.00am Invited Lecture -
Prof. M.F. Refojo (Dept. of Ophthalmology, Harvard University, USA) -
"Properties and Applications of Ophthalmic Biomedical Polymers".

9.40am -
J.Newton-Howes, T. Grant, A. Back and B.A. Holden (CCLRU, University of N.S.W., Aust.) - **"Prediction of the Movement Characteristics of Soft Contact Lenses".**

10.00am - Morning Tea

Chairman - Bill Reid

SESSION 10. GENERAL BIOMEDICAL POLYMERS
10.30 -
Prof. P. Giusti and F. Ciardelli (University of Pisa, Italy) - **"Bio-artificial Polymeric Materials".**

11.10am -
P.E. Duncan (Paladin Medical Stillwater MN, USA) -
"Polymer - Matrix Rare-earth Magnets for Medical Applications".

11.30am -
B.Jansen (Hygiene Institute, University of Cologne, FRG) - **"Modification of Polymers for the Prevention of Foreign Body Infection".**

11.50am - Lunch

1.15pm - Allied Institutions Visits

7.00pm - SYMPOSIUM BANQUET

Banquet Guest Speakers
8.00pm DR. D.J.T. Hill - Chairman, RACI Polymer Division

8.30pm Mr. David Parker - Deputy Premier

End Day 3

THURSDAY 9 FEBRUARY, 1989.

Chairman - Geoff Richardson

SESSION 11. GENERAL BIOMEDICAL POLYMERS
9.00am
Yu.G.Gololobov (Academy of Sciences, USSR) - **"A New Approach to Protection of Bioprosthesis from Bacterial Infection".**

9.20am -
H.J. Greisser, J.H.Hodgkin and E. Rizzardo (CSIRO, Chemicals and Polymers, Melbourne, Aust.) - **"Plasma Surface Treatment and Polymerization for Production of Biocompatible Surfaces".**

9.40am -
Prof. N.A.Peppas and M.L. Brannon (Chemical Engineering, Purdue University, USA) - **"Temperature Sensitive Hydrogels for Biomedical Applications".**

10.00am - Morning Tea

Chairman - Wayne Spencer

SESSION 12. GENERAL BIOMEDICAL POLYMERS
10.30am -
M.F.Sigot-Luizard (Universite de Technologie de Compiegne, France) - **"An in Vitro Model of Quantitative Cyto-compatability Assessment Relevant to the Different Classes of Biomaterials".**

10.50am -
J.Klier and N.A.Peppas (Chemical Engineering, Purdue University, USA) - **"Ampholytic Hydrogels Sensitive to Physiological Conditions".**

11.10am -
Dr. Chris C. Berndt, P.J. Callus and G. Jessup (Dept.Materials Eng. Monash Uni., Aust.) - **"The failure Analysis and Material Properties of Sutures".**

11.30am Invited Lecture -
Prof. P.C. Farrell (University of N.S.W. and Baxter Centre for Medical Research, Aust.) - **"Synthetic vs Natural Membranes".**

12.10 - Lunch

Chairman - Grant Ferguson

SESSION 13. POLYMERS IN CARDIOVASCULAR SURGERY

1.20pm Invited Lecture -
Prof. R.E. Marchant and D. Yu (Depts. of Biomedical Eng. and Macromol. Science, Case Western Reserve University, Ohio, USA)- **"Preparation of Biomedical Interface Materials Using Radiofrequency Plasma Polymerization".**

2.00pm -
A.K.Podolsak and G.Roberts (Bio Nova Neo Technics Pty. Ltd., Melbourne, Aust.) - **"Criteria for Evaluating New Synthetic Biomaterials for Use in Vascular Grafts".**

2.20pm -
J.G. Steele, W.D.Norris, P.A.Underwood and G.Johnson (CSIRO, Division of Biotechnology, NSW, Aust.) - **"The Relative Contribution of Fibronectin and Vitronectin to Endothelial Cell Adhesion on Chemically Defined Substrates".**

2.40pm - Conclusion

BIOGRAPHICAL NOTES ON KEYNOTE SPEAKERS

Harry Oysaed:
Received his cand.real degree (PhD) from the University of Oslo, Norway and joined NIOM-Scandinavian Institute of Dental Materials as a Research Associate. He serves on the Board of Directors of the Norwegian Chemical Society, Section for Macromolecular Chemistry. His research interests include fracture and viscoelastic properties of multiphase acrylic systems, conversion during polymerization and adhesion of methacrylate-based polymers to different inorganic materials.

Martin J.Tyas:
Is Director of the Australian Dental Standards Laboratory, Melbourne, Australia. He holds a number of other prominent consulting appointments and is an active member of various committees. His academic qualifications include BDS and PhD from University of Burmingham, UK; Grad. Dip. Health Science (Health Management), WAIT; Prov. Assoc. Australian College of Health Service Administrators and is a Fellow of the Academy of Dental Materials.

Martin is a member of the Australian Dental Assoc., Aust. Soc. for Forensic Dentistry, Forensic Science Society, International Assoc. for Dental Research and the International Dental Federation. Several professional appointments both in Australia and the UK have given him a varied career. He has published over 60 papers.

Wayne D.Cook:
Is a graduate of the University of Melbourne holding both a BSc (Hons) and PhD. He joined the Commonwealth Department of Health, Medical Devices and Dental Products Branch and presently Head of Chemistry. He has studied a wide range of elastomers, semi-

crystaline glasses, ionic and covalently linked network polymers. His studies have concentrated on the relationships between polymerization kinetics, structure, rheological behaviour and mechanical properties. He has also undertaken research into colour measurement and spectroradiometry.

Wayne has lectured to a number of UK and USA Universities and manufacturing companies. He has visited China as part of an ADAB-sponsored collaborative project between MDDP and the Beijing Medical University designed to encourage the development of modern dental materials by Chinese industry. His current research interest is the influence of network structure on fracture behavior.

Stuart L. Cooper
Chemical Engineering Department
The University of Wisconsin, Madison, USA.

Research Interests:
Polymer Science and Engineering, Structure Property Relations of Polyurethanes, Ionomers, Blends and Block Polymers, Mechanical and Dielectric Spectroscopy, X-Ray Scattering, EXAFS Analysis of Ion Containing Polymers, Polyurethane Biomaterials, Blood-Material Interactions.

Professor Cooper obtained his Degree in Chemical Engineering from Massachusetts Institute of Technology and his PhD. from Princeton University. Since obtaining his PhD he has held a number of Professorial posts from Assistant Professor to his current position of Departmental Chairman. He is the recipient of many honours awards and also been a very active member of a number of professional societies and associations.

Stuart has served on many advisory boards and panels and currently holds office on the Mattson Institute for Spectroscopic Research, Scientific Advisory Board and J. Biomaterials, Polymed Edition, North American Editor. His busy schedule has still allowed him to publish over 170 articles and over 30 review articles and book chapters.

H. Daniel Wagner:
Obtained his BSc. from the Free University of Brussels, Belgium and both MSc. and PhD from the Hebrew University, Israel. He worked as a Postdoctoral Associate for two years in the Department of Mechanical and Aerospace Engineering at Cornell University, USA followed by Postdoctoral Fellow at the Weizmann Institute's Department of Materials Research. Daniel received the Levi Eshkol Fund for Postdoctoral Research awarded by the National Council for Research and Development, Ministry for Science and Development. He holds the J. and A. Laniardo Career Development Chair in Industrial Research.

Miguel F. Refojo:
Is Head of the Biomedical Polymers Laboratory at the Eye Research Institute of Retina Foundation and Associate Professor of Ophthalmology at Harvard Medical School, Boston, MA, USA. For over 25 years, Dr. Refojo has published widely on biomedical polymers and their physiological interactions with eye tissues and has often lectured on contact lenses, sustained delivery devices, surgical adhesives and implants in ophthalmology. He has been a Visiting Professor at the College of Optometry, University of Houston; Visiting Scientist at the Cornea and Contact Lens Research Unit of the University of New South Wales and is past President of the International Society for Contact Lens Research. Dr. Refojo was co-founder and Director of Corneal Sciences Inc. which developed the CSI contact lenses. He has developed scleral buckling materials, vitreous implants, artficial corneas, sustained delivery devices and was responsible for the use of cyanoacrylate adhesives in ophthalmology. He is also a consultant to private industry and government agencies.

Nicholas A. Peppas:
Received his Dip. Eng. from the National Technical University of Athens, Greece and his Sc.D. from the Massachusetts Institute of Technology both in Chemical Engineering. He is currently Professor of Chemical Engineering at Purdue University but has held a number of Visiting and Adjunct professorial positions in the USA and Europe.

He is the author of over 320 publications, 6 books and patents. Dr. Peppas is the editor of the Journal "Biomaterials", the Ch.E. Monographs of Elsevere and a member of the editorial boards of J.Applied Polymer Science, J. Controlled Release, Biomedical Polymers, Polymer News, STP Pharma and J. Biomaterials Research, Polymer Edition. He was the recipient of the 1988 Curtis McGraw Award of ASEE, the 1984 Materials Award of AIChE, the 1982 Zyma Foundation Award for the Advancement of Medical and Biological Sciences, the 1980 ASEE Western Electric Fund Award, the 1982 AIChE Award, Potter Award (1978, 1985) and the Shreve Award (1978, 80, 82, 85). Dr. Peppas is a member of the New York Academy of Sciences, AIChE, ACS, APS, SPE, ASAIO, ISAO, ASEE, AAAS and other societies. He was the 1987-88 President of the Controlled Release Society.
His research interests include molecular structure of polymers, solute diffusion polymer films and membranes, solvent transport in glassy polymers, controlled release, biomedical applications of polymers and biointerfacial phenomena.

Professor Roger E.Marchant
Department of Biomedical Engineering
Case Western Reserve University, Ohio, USA.

Research Interests:
The behavior of polymers at biological interfaces, including biodegradation and biocompatibility phenomena; the application of polymers for use as biomaterials; radiofrequency plasma polymerization and the modification and characterization of material surfaces.

Professor Marchant obtained his BSc.(Hons). from the University of Sussex, England and his PhD. from Case Western Reserve University, USA. He received the award for Outstanding Research (PhD category) at the 2nd World Congress on Biomaterials in April 1984. Roger was Co-Chairman of the 3rd World Congress on Biomaterials in 1988 and is the Associate Editor J.Biomedical Materials Research. He has published over 25 articles on biomedical polymers.

PAPER SUMMARIES

HYDROGELS AT BIOLOGICAL INTERFACES

B.J.Tighe,
Speciality Materials Research Group
Aston University, Birmingham B4 7ET, UK.

The effective design of hydrogels for contact lenses demands an understanding of structure-behaviour relationships in terms both of physical properties and of biological interaction with the ocular environment. For several reasons the eye provides a valuable body site for "in vivo" studies of biological interactions of polymers . The composition of tears is complex and mimics many aspects of other body fluids. The ease of insertion and removal of a contact lens enables the very early stages of the interaction process to be studied without the associated problems of surgical trauma. Similarly, the use of extended wear schedules enables aspects of prolonged biological contact to be studied.

The development and use of techniques that enable the early stages of ocular interaction to be studied will be discussed, and in particular the role of lipids in the biological interface conversion processes that lead to long term spoilation of ocular biomaterials.

EFFICIENCY OF PROTEIN REMOVAL SYSTEMS FOR SOFT CONTACT LENSES.

Joanne Rechberger, BSc, Tim Grant BOptom, Deborah Sweeney BOptom and Brien A Holden PhD. Cornea and Contact Lens Research Unit, School of Optometry, University of New South Wales, Sydney NSW, Australia.

The relative efficiencies of four commercially available cleaning systems for contact lenses have been determined quantitatively. The amounts and quality of protein accumulated on lenses treated with these systems were compared with an untreated control group. Medium water content lenses worn continuously for one week were used. Quantitative analysis was performed using a modified Lowry Protein assay. The Rudko Classification System (prior to protein assay) and electron microscopy were employed. When treated according to manufacturers' specifications, enzymatic (137 ± 100ug/lens) and standing wave systems (146 ± 84ug/lens) were more effective in reducing protein level in this lens type than ultrasonic (305 ± 111 ug/lens) or friction (608 ± 81ug/lens) cleaning methods. The control group yielded 760 ± 169ug/lens. The molecular and physical mechanisms underlying these differences are examined.

IN VITRO CYTOCOMPATIBILITY ASSESSMENT OF BIOMATERIALS TOWARD GINGIVAL TISSUE BY ORGAN CULTURE METHOD : APPLICATION TO DIFFERENT DENTAL MATERIALS

M. LETORT and M.F. SIGOT-LUIZARD
Laboratoire de Biologie cellulaire Expérimentale
Université de Technologie de Compiègne.
Boite Postale 649 - 60206 COMPIEGNE FRANCE

The classification requirement of the different properties of dental materials has been pointed out very early by clinicians. Therefore, in vivo and in vitro researches have been performed to evaluate mechanical and biological properties of such materials. Our aim has been to fit to gingival tissue specifications an organ culture method originally described for ophtalmic and vascular materials evaluation.After having characterized the tissue, the method has been performed. It is based on the analysis of 3 properties involved at the tissue material interface: Cell migration, multiplication and adhesion. Some different dental materials (metals, alloys, resins, Hydroxyapatite, and a plastic control) have been evaluated. Assessments have been performed for any material both by direct contact and in contact of extracts of the material in the culture medium. Results have been reported onto two diagrams to compare the very different behaviours and deduce their biofunctional implications.

CHARACTERIZATION OF MULTIPHASE METHACRYLATE BASED POLYMERS AND COMPOSITES FOR DENTAL APPLICATION.

Harry Øysæd, NIOM - Scandinavian Institute of Dental Materials, P.O.B. 70, N-1344 Haslum, Norway.

Knowledge of the chemical composition of dental materials is essential to the understanding of their clinical and biological as well as their physical and chemical properties. Characterization of the chemical composition of dental polymers may be obtained by use of different chromatographic (GC, HPLC, GPC) and spectroscopic (IR, UV, NMR, MS) methods.

Multiphase methacrylate based polymers are commonly used in dentistry. Unfilled polymers are primarily used in prosthetic dentistry, whereas filled resins are employed for restorations. The mechanical properties of the polymerized materials are influenced by the final structure of the organic phase as well as the content and type of filler.

The components leaching out of a polymerized material are essential for its biological properties. These components may be unreacted parts of the original formulation or degradation products. By using various analytical methods, it has been possible to identify and quantify potentially allergenic component of dental polymers.

SOFT POLYMERS IN PROSTHODONTICS

Peter Mack
The Dental School
University of Western Australia

Biomedical polymers intended for use beneath dental prostheses should replicate the rheological properties of the mucoperiosteal tissues of the mouth.

Additional properties required of such materials are those of adequate long term dimensional stability, biological compatibility and social acceptance in terms of taste and colour.

The Youngs' modulus of a number of successful soft dental polymers was determined to be in the order of 3 x 10 n.m -2.

The modulus is sensitive to the rate of load application. This applies both during the initial plastic and later elastic stages of gellation.

In clinical practice and under test the material barrells under load. The compression modulus of test samples can be related to the clinically perceived Youngs modulus by application of various shape factors.

The pressure distribution over near cylindrical edentulous ridges was assessed. To be of value in their intended function of cushioning dental loadings applied across a denture onto a traumatised or atrophic mucoperiosteal base a minimum thickness of 3.0 mm. is recommended.

CARBON/GRAPHITE FIBER REINFORCED POLY(METHYL METHACRYLATE) FOR IMPLANT-FIXED DENTAL BRIDGES.

Karl Ekstrand and I.E. Ruyter, NIOM, Haslum, Norway.

Dental prostheses (bridges) which are fixed to the jaw by titanium implants are usually made of expensive gold alloys. Carbon/graphite (C/G) reinforced poly(methylmethacrylate) (PMMA) has been investigated as a potential material for bridge construction. C/G reinforced PMMA was assessed with regard to flexural properties and the adhesion between the fibers and the matrix. Emphasis was placed on the effects of storage of the C/G-PMMA material in air or water. Both unidirectional and braided tubular fibers were used. Compared with storage in air, storage in water caused a decrease in fracture stress and flexural modulus when commercially available fibers were used as reinforcing material. Composites with cleaned and specially surface treated fibers had only minor differences in flexural properties after dry and wet storage. Based on the in vitro investigations, a method for processing dental bridges of C/G fiber reinforced PMMA on titanium implants was developed. A clinical study comprising 40 patients with C/G fiber reinforced bridges has been performed, and the results after 4-5 years of observation are favorable.

CLINICAL USE OF COMPOSITE RESINS IN DENTISTRY

M J Tyas, Director, Australian Dental Standards Laboratory, Australian Department of Community Services of Health, 240 Langridge Street, Abbotsford, Victoria 3067, Australia

Prior to the mid 1960s, unfilled polymethylmethacrylate (PMMA) had been used for restoring teeth, with generally unacceptable results. The synthesis of specialized dimethacrylate resins led to the commercial availability of filled resins with improved properties. More recent developments have been the introduction of photocured materials with higher filler loadings, resulting in more acceptable clinical performance. However, of particular concern is the integrity of the material/tooth interface, and although good micro-mechanical bonding of composite to tooth enamel can be achieved, effective bonding to dentine remains questionable. There are also concerns regarding the wear resistance of composites in the posterior teeth. These two aspects will be discussed in detail.

DENTAL RESTORATIVE MATERIALS - STRUCTURE AND PROPERTIES.

Dr Wayne D Cook, Medical Devices and Dental Products Branch, Dept. of Health, 240 Langridge St, Abbotsford, Vic, Australia 3067.

Numerous types of polymers are utilized in dentistry ranging from soft elastomers, to glassy, rigid networks. With the exception of bone cements, these materials are unique in the biomedical field because they are manipulated in a fluid form by the clinician and then rapidly polymerized to the final state. For the last five years, the primary materials research in dentistry has concentrated on dimethacrylate based composite resins and cation-crosslinked poly(alkenoate) materials (glass ionomers) as replacements to silver-amalgam restoratives.

This lecture will first review the composition, polymerization kinetics and structure of composite resins and and glass ionomers and then describe how the structure influences the fracture behaviour and therefore the wear of these materials.

Future developments in this field including the use of expanding unsaturated spiro-ortho carbonates, fluorinated monomers, new filler systems, truly adhesive restorative materials and hybrid ionic-covalent networks will be briefly discussed.

PROTEIN ADSORPTION ON POLYURETHANE BIOMATERIALS: The role of Vitronectin in Blood-Surface Interactions

Stuart L. Cooper

The composition, conformation and biological activity of proteins in the adsorbed protein layer that forms upon blood contact with a biomaterial surface is being characterized in order to understand the influence of polymer properties upon the success of a biomaterial. This research specifically focuses upon determining the role of the plasma protein vitronectin in the adsorbed protein layer. Vitronectin, a cell adhesive protein containing the RGD tripeptide sequence, has the potential of readily establishing a position in the adsorbed protein layer and of stimulating thrombosis and related phenomena. Its adsorption to various surfaces and the promotion and/or extinction of its various activities upon adsorption to different surfaces is being studied.

THE EFFECT OF ALBUMIN COATING ON THE IN VITRO BLOOD COMPATIBILITY OF DACRON ARTERIAL PROSTHESES

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The effect of albumin coating on the thrombogenicity of Dacron vascular grafts was investigated using a recirculating, in vitro perfusion system containing fresh human donor blood. The evaluation involved a comprehensive analysis of platelet activation, encompassing platelet count, release, aggregation, and platelet adhesion. Fibrin formation was assessed by measuring fibrinogen levels and fibrinopeptide A production; leukocyte interaction was analyzed by measuring total leukocyte concentration, and cell adhesion to the graft surface was assessed by scanning electron microscopy. The albumin coating provided a film-like covering for the Dacron with little change to the graft topography, although the coating appeared brittle and showed evidence of flaking. The results of all the in vitro characterization methods employed in this study showed that the albumin coating significantly improved the short-term blood compatibility of Dacron. These data provide evidence indicating that surface modification of a biomaterial can have a profound influence on its blood compatibility.

THE TENSILE PROPERTIES OF VASCULAR PROSTHESES

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A difference in compliance between the graft and the natural artery will cause stress at the point where they are sutured together and failure may result. The compliance and fracture loads of the graft was examined by means of longitudinal tensile tests. Both knitted dacron mesh alone and the mesh reinforced with collagen were tested.

The properties of the meshes used to manufacture artificial arteries were consistent. The collagen in the vascular graft failed at a variety of loads which were all well above the natural artery strength. This test method may be used to determine the thickness and quality of collagen on the graft.

FAILURE OF VASCULAR GRAFTS: CORRELATION WITH STRUCTURE AND MATERIAL PROPERTIES

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In the present study a critical review of the structural and material factors contributing to the mechanical breakdown of arteries and artery/implant composite systems were analyzed. The most important causes of graft failure were underlined as well as the time to failure and relative frequency of each failure mechanism, by means of the Weibull failure probability model, which was applied to vascular graft failure data reported over a period of 30 years. The main objective of this analysis was to attempt to separate out the various modes of failure of vascular grafts occuring at various times under physiological stresses using statistical tools. Future research areas important for characterizing the mechanical behaviour of artery/implant systems are suggested, with the aims of establishing rational standards for prosthesis evaluation.

POLYMERIC ENDOLUMINAL PAVING\SEALING: A Biodegradable Alternative to Intravascular Stenting Marvin J. Slepian and Anton Schindler Research Triangle Institute, Research Triangle Park, N.C.

Intravascular stents are promising endoluminal devices for the maintainence of vessel patency post angioplasty. Current stents, either metal or polyolefin, carry the limitation of being permanent and irretrievable. We developed a new technique in which a bioresorbable polymer could be deployed intravascularly as a thin film seal. A balloon tipped catheter allowing for controlled mechanical and thermal deformation facilitated polymer application. Ten latex mock vessels (I.D.=3.0mm), 12 isolated perfused (70 mmHg) bovine coronary arteries (I.D.=2.8±0.3mm), and 6 in situ canine carotid arteries (I.D.=2.9±0.2mm) were purposely overdistended and polymer sealed at 4mm. I.D. (15 mm lengths). Contiguous vessel segments subjected to identical catheter deployment conditions, w/o polymer, served as controls. Vessels were fixed, sectioned and vessel I.D. and % luminal surface in contact with polymer (paving) measured at 250x. All polymer sealed vessels remained "dilated" (I.D.= 4.0±0.1 mm) with luminal paving of >90%. Unsealed vessels did not remain dilated. Thus, vascular endoluminal surfaces may be intimately sealed with a biodegradable polymer with adequate structural stiffness to effectively maintain a selected internal diameter.

Polymer Composites for Orthopaedic implants

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This project was developed from work on water emulsified epoxy resins and the reinforcement of these as potential orthopaedic implant materials. However, for load-bearing devices conventional systems are required and attention turned to use of pre-preg to make laminated composites. Type II fibre was used in a heat hardening resin system. Two aims in the programme were to attempt to reduce the effects of stress protection in bone arising from use of stiff metallic implants and to provide better fatigue life. Following in vivo functional testing in sheep, human trials were begun for tibial fractures and have been reported. Approximately 30 fractures were so treated and in all cases satisfactory healing was obtained. Stainless steel screws were used. The trial has now been extended to forearm fractures for which this is more clearly a recommended treatment and satisfactory stability and healing have been obtained. The level and type of activity in the forearm is quite complex and results may in fact show a relationship to these factors. The healing pattern is distinctively different from that seen in the tibia but this may be an effect of the relative stiffness of the two different systems. Degradable composites of polyhydroxybutrate and glass or hydroxyapatite are now under investigation.

SELECTION OF POLYMERIC MATERIALS FOR COSMETIC HAND PROSTHESIS

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Prosthesis nowadays no longer just function well mechanically but they also look real. This is especially true for the cosmetic hand prosthesis which looks like real hand in terms of shape, colour, texture and other physical attributes. The selection of polymeric materials becomes the critical part in providing the aesthetic appearance and durability of the cosmetic hand prosthesis. It requires the study of the structure of human skin, identification of basic requirements to meet the functionality of the hand, and an objective procedure in materials selection. This paper describes this procedure which involves the derivation of weighting factors using a digital logic approach and the material performance index which gives a numerical value where upon an objective decision can be made. From this method, silicone rubber was concluded to be the best compromised material. This paper also traces the history of cosmetic hand prosthesis, discusses the material properties of various polymers and projection of future trends which appears to be dominated by computer aided engineering.

DIFFUSIVE AND SURFACE PROBLEMS DURING UTILIZATION OF HYDROGELS IN OPHTHALMOLOGY

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The oxygen permeability through hydrogels utilized in contact lenses is determined and analyzed using novel diffusive models. It is shown that the polymer structure influences the oxygen diffusion coefficient. Partition effects are also important in oxygen permeation as indicated by surface analysis. Results using PHEMA, PVA, PNVP and their copolymers with hydrophilic and hydrophobic moieties will indicate this behavior.

PROPERTIES AND APPLICATIONS OF OPHTHALMIC BIOMEDICAL POLYMERS

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Biomedical polymers, used as contact lenses (CL) and surgical implants, are important in modern ophthalmology, as are reconstituted and/or chemically modified biopolymers. Implants are used for optical correction in the cornea and as intraocular lenses (IOL), for treating glaucoma, and in retinal detachment surgery for scleral buckling and as vitreous implants. Adhesives are particularly useful for treating corneal perforations. Ophthalmic polymers have specific physical and physiologic requirements, such as transmission of visible light and filtration of UV light for CL and IOL, O_2 permeability and tear wettability for CL, high interfacial tension, and viscosity for certain intravitreous implants, etc. Hydrogels, glassy and elastomeric biomedical polymers, viscous hydrophobic polymers and viscoelastic biopolymers solutions, as well as monomers that polymerize in situ have applications in ophthalmology.

PREDICTION OF THE MOVEMENT CHARACTERISTICS OF SOFT CONTACT LENSES

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The on-eye fitting characteristics of a soft contact lens (movement, lag and centration) influence vision and the removal of metabolic waste products from the cornea. The aim of this study is to show how the mechanical properties of the material from which a contact lens is made can be used to predict the performance of the lens.

A series of contact lenses have been manufactured in the same design by a single lathe operator from a range of different materials. The movement characteristics of the lenses were determined in a masked clinical trial. Young's modulus and the stress relaxation modulus were then determined by measuring the pressures developed under an inflated lens. The relationship between the mechanical properties of the material and the performance characteristics of the lens is discussed.

BIO-ARTIFICIAL POLYMERIC MATERIALS

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Polymeric materials for biomedical applications should possess both chemico-physical and mechanical properties which are adequate to the end use, and opportune biocompatibility.

Many polymers already on the market show chemico-physical and mechanical properties comparable with those of biological materials they must substitute, but they do not show sufficient biocompatibility

On the other hand biological polymers (fibrinogen, collagen etc.) show, of course, good biocompatibility but often inadequate mechanical properties and high production costs

We had the idea to design new biomaterials based on blends or composites consisting of biopolymers and artificial (synthetic) polymers

This lecture will describe the results obtained in the study of a new biomaterial produced by mixing synthetic polyurethanes with the plasma protein fibrinogen and subsequently transforming the fibrinogen into covalently cross-linked fibrin by the enzymatic treatment with thrombin, factor XIIIa and calcium ions

This material has been successfully used for the production of small diameter vascular grafts and nerve guidance channels

Other potential bio-artificial polymeric materials will be illustrated.

POLYMER-MATRIX RARE-EARTH MAGNETS for MEDICAL APPLICATIONS.

P. Elaine Duncan, Paladin Medical, Stillwater, MN, USA. Industrial applications of polymer-matrix magnets are well known and highly developed, but medical device applications for these versatile magnetic materials have not developed. Lower magnetic strength when compared to sintered magnets has limited the desirability of these magnets in many medical applications, but the potential versatility of design with a variety of polymers as the matrix and the ability of the polymer-matrix to reduce bio-corrosion of the cobalt-based rare-earth magnetic particles should encourage their utility. Several formulations of polymer-matrix magnets have been studied for magnetic flux-density stability in an in-vitro aging study. Analysis for corrosion and cytotoxicity has been conducted. Cross-sectional SEM's illustrate the inherent properties of the polymer-matrix magnet to isolate the magnetic components from contact with tissues and body-fluids, enhancing their biocompatibility. These factors coupled with the versatile fabrication techniques should be an encouragement to future medical device applications.

A NEW APPROACH TO PROTECTION OF BIOPROSTHESIS FROM BACTERIAL INFECTION.

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A new approach to protection of bioprosthesis from calcification and bacterial infection which is based on creation of condition of "self-destruction" of microorganism on the surface of tissue is studied. The conditions are created by a protective layer of a crosslinked hydrophilic polymer which contains a covalently bounded antibiotic. A type of polymer is of primary importance. Being highly stable towards enzymes the polymer should be lible to destruction by bacteria which leads to release of the free antibiotic. As a result of this study optimal conditions cell, highmolecular protein and enzymes aggression, but not interfering with the salt metabolism bitween the blood and prosthesis. Such a protection leads to the reductions of calcification of prosthetic tissue in vivo.

Plasma Surface Treatment and Polymerization for Production of Biocompatible Surfaces

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Gas discharge technologies have been explored for surface modification of polymeric materials intended for biomedical applications. Exposure of polymer surfaces to a gas plasma creates surfaces with different chemical groups and degree of hydrophilicity. In non-depositing plasma atmospheres, new chemical groups are introduced into the very surface only. Fluorocarbon polymers are made wettable by exposure to an air or oxygen plasma, and the growth of endothelial cells is improved. In polymerizing plasmas, organic-polymeric thin films are produced. A range of organic vapours (gas or boiloff from liquid) have been found to be useful for production of high quality polymeric thin films. Due to the short range nature of interfacial forces, only the plasma polymer film is seen by the biomedical environment, and its chemical structure governs the biomedical interactions. Endothelial cell growth experiments indicated a great improvement in biocompatibility for some of these films.

AN IN VITRO MODEL OF QUANTITATIVE CYTO-COMPATIBILITY ASSESSMENT RELEVANT TO THE DIFFERENT CLASSES OF BIOMATERIALS

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The cytocompatibility assessment of biomaterials has been defined by measuring "in vitro" three biological parameters involved at the interface tissue-material (cell growth, migration and attachment). Computerization of the data makes the model reproducible and easy to apply. For each class of biomaterial (cardio-vascular, orthopaedic, dental and ophtalmological) we used the tissues belonging to the future implantation site, that are respectively endothelium, cartilage, gingival and cornea, with reference to positive (toxic) and negative (non toxic) control materials. The tissue is cultivated in direct contact with the biomaterial and in contact with its extract. We obtained different responses depending on the tissue and/or the biomaterial used, that demonstrates the sensitivity of the model. Both extracts and direct contact studies allow to define respectively the cytotoxicity of the biomaterials and to preselect it as a function of their biological requirements.

TEMPERATURE-SENSITIVE HYDROGELS FOR BIOMEDICAL APPLICATIONS

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Abrupt changes in the network structures of biocompatible hydrogels have been observed as the experimentation temperature approaches the critical (theta) temperature of the system. Such gel collapse may lead to expulsion of a portion of an incorporated drug from a hydrogel, due to a major and abrupt change of the mesh size. It is shown that the amount of drug released is related to the reduced temperature, $\theta = (T - \Theta)/\Theta$, and the molecular size of the network. Experimental studies with various acrylamide-containing hydrogels showed this dependence.

MODIFICATION OF POLYMERS FOR THE PREVENTION OF FOREIGN-BODY INFECTIONS

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Infection of medical devices and implant materials has become a severe problem in modern medicine. We have developed some approaches for the prevention of such infections by modification of the device or implant material. Surface modification of polymers by glow discharge treatment as well as loading of polymers with antimicrobial drugs are used to inhibit bacterial adhesion to the polymer surface which is regarded as the first important step in the pathogenesis of such infections. Glow discharge grafting of polyurethanes with hydrophilic monomers resulted in a decreased bacterial adhesion. These surfaces also adsorb preferentially albumin which leads to a further reduction in bacterial adhesion. Experiments with polyurethanes loaded with various antibiotics (oxacillin, clindamycin, gentamicin) show that initial adhesion of grampositive and gramnegative bacteria is not inhibited, but after 24 - 48 h a significant reduction of adherent viable bacteria can be observed.

COMPLEX-FORMING HYDROGELS SENSITIVE TO PHYSIOLOGICAL CONDITIONS

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Hydrogels consisting of graft copolymers of poly(ethylene glycol) on poly(methacrylic acid) backbone chains were synthesized. These networks exhibited large changes in swelling and solute permeability with small changes of pH, temperature or composition of the swelling medium. The dependence of swelling, mechanical and diffusive properties was studied for a variety of molecular parameters, including the molecular weight of the pendant chain, the copolymer composition and the crosslinking density.

SYNTHETIC vs NATURAL MEMBRANES

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The human body employs a bewildering array of membranes for the concentration, separation, and purification of vital fluids to maintain homeostasis. Artificial organs rely upon synthetic membranes as surrogates for the same purpose. To date, and as far into the future as one might reasonably forecast, man-made membranes are and will remain primitive and crude by comparison with the structural elegance, selectivity, and fluid-pathway efficiencies of naturally occurring membranes. Nevertheless, existing membrane technology has provided a satisfactory basis for several artifical organ systems: *hemodialysis* with homogeneous cellulose membranes for replacement of kidney function; *oxygenation* with porous or gas-permeable matrices for pulmonary replacement during surgery, and *plasmapheresis* with microporous membranes for harvesting of plasma from whole blood for treating various debilitating diseases. Despite shortfalls in man's attempts to mimic nature's elegant membrane systems, these aforementioned procedures provide life-saving benefits.

In another context, continuous ambulatory peritoneal dialysis (CAPD) has recently emerged as a successful alternative to hemodialysis and one which relies upon natural rather than synthetic membranes; data is now beginning to accumulate which will allow direct comparison between the two prosthetic modalities for treatment of kidney dysfunction.

Present and future developments in membrane systems for clinical applications will be compared and contrasted.

PREPARATION OF BIOMEDICAL INTERFACE MATERIALS USING RADIOFREQUENCY PLASMA POLYMERIZATION

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Blood and tissue compatibility are major concerns in the performance of existing biomedical materials. The surface, or interface, of the biomaterial is one of the most important factors that determines its biocompatibility. However, the optimum bulk properties of existing biomaterials are rarely coincident with optimum surface (interface) properties. Consequently, any improvement is dependent upon the ability to optimize the material's surface without adversely affecting its bulk properties. Surface modification using radiofrequency plasma (glow discharge) synthesis methods is a surface specific approach, inherently suitable for achieving these goals, with a wide range of blood or soft-tissue contacting materials. Our recent studies have been directed toward realizing the outstanding potential of this technique for preparing new biomedical interface materials. The results of our preliminary studies, which have included the preparation and characterization of hydrophobic and hydrophilic plasma polymerized films deposited on both polymeric and non-organic substrates, will be presented.

"CRITERIA FOR EVALUATING NEW SYNTHETIC BIOMATERIALS FOR USE IN VASCULAR GRAFTS"

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Synthetic biomaterials are being successfully used in a variety of surgical prostheses. Any material to be used as a blood contact surface needs to be biocompatible, non-thrombogenic and should not activate platelets. Further, as a vascular graft, the tube needs to have compliance and elasticity compatible with the host artery; it should also have adequate suture retention characteristics. The use of these and other performance criteria in the evaluation of promising new biomaterials in the context of extensive data obtained in establishing a biosynthetic graft (OMNIFLOW) as a clinical vascular prosthesis will be discussed.

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HYDROGELS AT BIOLOGICAL INTERFACES

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Synthetic hydrogels (which may be conveniently described as water-swollen polymer networks) are a versatile range of materials which are of potential value in many biomedical applications. Some of these, such as contact lenses, drug delivery systems and wound dressings are now well established. Others, such as liver support systems, permselective sensor membranes and cell culture substrates have been less thoroughly investigated. Work it these laboratories has been concerned with two broad areas. The first is directed towards a structural understanding of the behaviour of hydrogels, together with the design of materials for specific applications. The second is the study of the interaction of hydrogels with particular biological environments. A selection of publications, illustrating this work, is listed below.

The most significant single property of a hydrogel is the equilibrium water content (E.W.C.). This results from the dominating influence that the water held within the polymer matrix has on the mechanical, surface and transport properties (such as permeability and permselectivity) of the hydrogel. In many applications the need to achieve particular levels of permeability for specific transported species is the primary factor in controlling the success of the device. Examples of this include extended wear contact lenses and artificial liver support (haemoperfusion) systems. The need to balance the volume fractions of water required for adequate oxygen permeability (in the former case) and bile acid or bilirubin transport and sorption (in the latter) with the mechanical properties necessary for satisfactory performance of the device present considerable problems in polymer design. In meeting these difficulties the question of water structure within the polymer matrix, in addition to the total water content, must be addressed.

Although the correlation of structure with performance in terms of transport and mechanical properties presents difficulties, these are much less severe than those encountered with surface properties. Surface properties of hydrogels are particularly difficult to measure, because of the dominating effect of water at the surface, and present the additional complexity of correlation with behaviour at the biological interface.

One major aspect of the problem here is the lack of a suitable "in vivo" model which will allow the important early stages of the interaction of
the synthetic material with the biological environment to be studied.

The effective design of hydrogels for contact lenses demands an understanding of structure-behaviour relationships in terms both of physical properties and of biological interaction. Such an understanding also provides a basis for extending hydrogel design to other applications. A lens for extended (i.e. overnight) wear may be considered as an extension of the cornea. Thus, the lens must allow the cornea to respire normally, it must resist the deforming force of the eyelid and it must permit a continuous tear film to be maintained on the lens, whilst minimising the accumulation of deposits. These factors can be discussed in terms of oxygen permeability, rigidity modulus and surface properties.

In addition, the eye provides a valuable environment for "in vivo" studies of biological interaction. The composition of tears is complex and mimics many aspects of other body fluids. The ease of insertion and removal of a contact lens enables the very early stages of the interaction process to be studied without the associated problems of surgical trauma. Similarly, the use of extended wear schedules enables aspects of prolonged biological contact to be studied.

The development and use of techniques that enable these early stages of ocular interaction to be studied will be discussed, and in particular the role of lipids in the spoilation process.

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EFFICIENCY OF PROTEIN REMOVAL SYSTEMS FOR SOFT CONTACT LENSES

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Deposit formation still remains one of the major problems associated with both daily and extended wear soft contact lenses.[1,2] The major components of deposits in soft lenses are denatured proteins, chiefly lysozyme. With contact lens wear, denatured proteins form a multi-layered tightly bound adherent film covering all or part of the lens surface. This film cannot be removed by simple surfactant cleaning. If not treated this protein layer will accumulate with wear leading to irritation, decreased vision, decreased lens life and patient dissatisfaction.[3,4] In addition to the above, the accumulation of protein is associated with giant papillary conjunctivitis.[5] This progressive condition can eventually lead to permanent discontinuation from lens wear.

A variety of protein removal systems are commercially available. They rely on different mechanisms to remove the accumulated protein. This study examined four such removal systems:

i. enzymatic - proteolytic activity,
ii. standing waves - vibration of resonant waves in saline,
iii. ultrasonic - vibration of ultrasonic waves in saline,
iv. friction - manual application of a coarse powder.

One hundred and fifty medium water content (58%) contact lenses worn on an extended wear basis (i.e. without removal) for one week were used. A modified Lowry protein assay was used to determine the protein level for each lens. Prior to the assay each lens was qualitatively assessed using the Rudko Classification Method.[3] This is a method of visual inspection of the lens under different conditions and magnifications. Selected lenses were analysed using scanning electron microscopy.

Preliminary results show that with this lens protein is more efficiently reduced by enzymatic treatment (136.9 ± 100ug/lens) and standing wave (145.4 ± 84ug/lens) than either ultrasonic (305.3 ± 111ug/lens) or friction (607.5 ± 81ug/lens) (untreated control group yielded 760 ± 169ug/lens).

The physical and mechanical basis of these results are disscussed.

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HYDROGELS AS BIOMATERIALS FOR INTRAOCULAR LENS IMPLANTS.

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Ever since Ridley implanted the first intraocular lens in 1949, surgeons have been modifying implants in an attempt to produce the ideal pseudophakos.
I believe that lens design has reached a stage of sophistication where significant advances are unlikely to be achieved by further modifications of haptic design.
An alternative is to consider intraocular lenses manufactured from new improved biomaterials other than PMMA.

One such group of biomaterials are Hydrogels which have potential advantages as an intraocular lens material when compared with PMMA.

The term hydrogel includes many different polymers which share the characteristic of containing significant quantity of water and being hydrophilic.
I chose polyHema which contains 38% water by weight for several reasons:

1) This material has been more extensively studied as a biomaterial, than any other hydrogel.

2) The chemical nature is such that the material should be resistant to biodegradation and more stable than other hydrogels to varying conditions of pH and temperature.

3) The pore size is much smaller than higher water content hydrogels which reduces the tendancy fork protein and other molecular interactions in the biological enviroment.

4) Finally the lower water content imparts a higher refractive index so that the optic thickness is reduced allowing easier folding .

When one considers the 5 fundamental questions regarding the suitability of a biomaterial, 38% polyHema has the appropriate physical and mechanical properties for an intraocular lens.

Hydrogels can be produced to an appropriate level of purity for implantation. The water content and permeability allows the extraction of any residual monomer during processing of the lens which is not possible with PMMA.

PolyHema is thermostable and can be autoclaved and therefore does not require Ethylene Oxide sterilization with its problems of E.T.O. residues.
Poly Hema does not induce any inflammatory cytotoxic or other adverse changes in surrounding tissue and finally has a chemical nature which should resist biodegradation.

With these concepts in mind I designed a posterior chamber implant which has been used clinically with good results over a 5 year period of follow up.

CHARACTERIZATION OF MULTIPHASE METHACRYLATE BASED POLYMERS AND COMPOSITES FOR DENTAL APPLICATION.

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Methyl methacrylate (MMA) monomer and its polymer are widely used in dentistry. Liquid monomeric MMA and prepolymerized poly(methyl methacrylate) (PMMA) are mixed and polymerized. Cross-linking agents like ethyleneglycol dimethacrylate (EGDMA) or butanediol dimethacrylate (BUDMA) are added to the monomer liquid to improve the mechanical properties. (1,2). The resulting multiphase system may be characterized by a combined use of chromatographic (GC, HPLC, GPC), spectroscopic (IR, UV, NMR, MS) and microscopic (SEM, LM) methods (3). The mechanical strength of multiphase acrylic systems is generally regarded as being lower than that of single phase cast or moulded materials (4). Furthermore, auto-polymerized materials are usually weaker and less creep resistant than heat-polymerized materials (1,5). In multiphase heat polymerized acrylic systems the critical strain value, $_c$, for the appearance of crazes at constant tensile stress increases with increasing quantity of cross-linking agent (6). However, in cross-linked auto-polymerized materials $_c$ is independent of the quantity of cross-linking agent. The heat-polymerized materials fail in a brittle manner, whereas the auto-polymerized materials fail in a ductile manner.

Since their introduction in the late 1960s, polymeric composite materials have been the preferred esthetic restorative material. Dental composites exist in a variety of formulations. They contain the following essential components: 1) a resin system comprising one or more oligo- or poly-functional methacrylate or acrylate monomers /oligomers, 2) an initiator system for free-radical polymerization under ambient conditions, 3) additives such as stabilizers for the storage stability of the unpolymerized system and the chemical stability of the polymerized system, e.g. color stability, 4) a reinforcing phase consisting of glass, quartz, amorphous silica, or other fillers, and 5) an interphase on the filler particles made by application of a coupling agent such as 3-methacryloyloxypropyltrimethoxysilane. Dental pit and fissure sealants, bonding agents and orthodontic adhesives have similar compositions except that they are unfilled or lightly filled materials. The structure of the polymer matrix depends on the

structure of the monomers and oligomers and their conversion (7). The structure of the matrix and type and quantity of filler particles determine the mechanical properties of the polymerized composite materials (8).

The components leaching out of polymerized material determine its biological properties. Unreacted monomers and additives may leach from the polymerized materials. Oxidation of methacrylate based polymers may lead to formation and release of small quantities of formaldehyde (9,10). Monomers, additives and formaldehyde are known to cause allergic reactions. Furthermore, hydrolytic degradation and oxidation may lead to leaching of other products of unknown composition. Monomer composition, as well as the variation in type and concentration of initiators, may play an important role in formation and release of formaldehyde. Heat-polymerized denture base materials release less formaldehyde than the auto-polymerized materials (9). Investigations of nine different composites show release of small amounts of formaldehyde during water storage (10).

Heat-polymerized materials have better properties than the light- and auto-polymerized materials that are available for biological applications today. Improving the efficiency of the initiator systems may give better polymers in the future.

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IN VITRO CYTOCOMPATIBILITY ASSESSMENT OF BIOMATERIALS TOWARD GINGIVAL TISSUE BY ORGAN CULTURE METHOD. APPLICATION TO DIFFERENT DENTAL MATERIALS

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The assessment of the different properties of dental materials has been requested very early by clinicians (1). Therefore, in vivo and in vitro researches have been performed to evaluate mechanical and biological properties of such materials. Our aim has been to apply to dental materials an in vitro assessment method (2) already performed for ophtalmic, vascular and orthopaedic materials. Different dental materials used in oral implantology have been evaluated. The following experimental conditions have been shown optimal for growing gingival tissue (3) :
Nutrient medium : Iscove (37%), L-Glutamin 2% (1%), Colt serum (10%), Tricin 2% (2%) and Bacto-Agar 1% in Gey solution (50%). Tissue samples collected from new born rat (3 days) in the zone of future gingival tissue are covered on the nutrient medium by the material to be assessed. After 10 days incubation (35°C), different computerized analysis have been performed to provide the following data: Migration area (diag.1), cellular density, adhesion behaviour as function of time during an enzymatic dissociation and an adhesion cell modulated index(4).

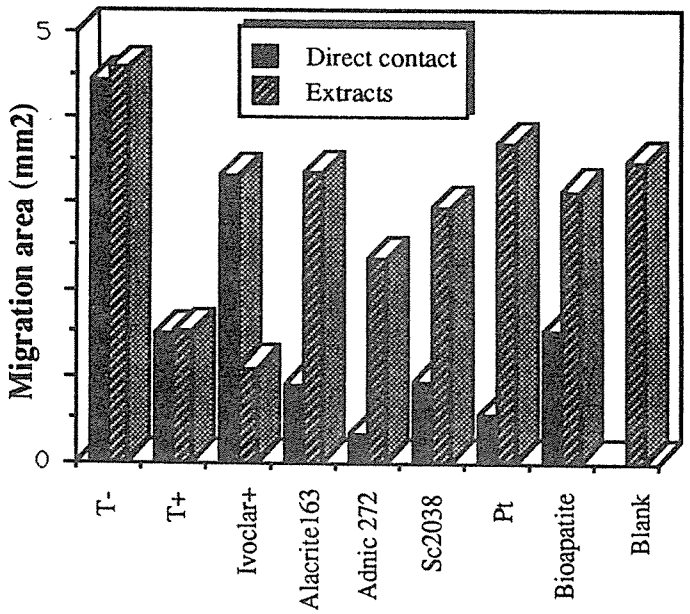

Diagram 1: Migration area of the different materials

The results have been reported on diagrams by plotting the cellular density as function of migration area and the adhesion behaviour as function of adhesion index, outlining thus the biofunctional involvements of the assessed materials.
Studies have been performed both by direct contact and on extracts of each material (5 days at 37°C in iscove medium - 5cm²/ml), the extraction liquid being then incorporated to nutrient medium. The extraction effect has been checked by a blank control.
The experiments have been performed on the materials referenced below :
Polymers (dental resin - Ivoclar+ ®), metal alloys (iron - SC2038 ®, cobalt - ALACRITE 163 ® and nickel - ADNIC 272 ®), pure metal (platinum) and hydroxyapatite (Bioapatite ®).
The results show a very significant difference between direct contact and extracts results. Direct cytocompatibility of polymer is effective when compared to controls, but extraction has eluted toxic products, as shown by the low migration area. Alloys and platinum appear cytostatic but the extraction study indicates the low toxicity of their released products.
Hydroxyapatite provides neutral results. The cell migration has not been enhanced by direct contact but released products appear as non toxic.

Conclusion:
Some very different behaviours have been pointed out in this study. Polymers and metals provide opposite results toward gingival tissue, considering our different indexes by this in vitro method. Therefore, the choice of the fitted material and manufacturing process appear as highly important in the selection of a biomaterial aimed for oral implantology.
Moreover, our protocol has been shown reproducible, precise and providing data which will have to be correlated with in vivo results.

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THE COMPLIANCE OF PROSTHODONTIC SOFT POLYMER MATERIALS.

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Masticatory loads in man are ideally transmitted to and resisted by sound teeth firmly attached to the bone of the jaws. For those who by age, accident or neglect are reduced to a completely artificial dentition, biting loads are borne by the oral mucoperiosteum. The penalty for such a change in tissue function is a decrease in chewing efficiency, and an increase in the incidence of oral pathological change.

In efforts to secure some measure of redistribution and reduction of locally damaging loadings transmitted by dental prostheses, increasing use has been made in recent years of prosthodontic soft denture polymer (SDP) materials.

The viscosity of an unset SDP material provides an indication of the ease with which a 'RTV' polymer will adapt to the tissue contours of the mouth. For the materials tested viscosity increases as the materials gel. The effect of temperature is determined by its influence on the overall viscosity of the polymers. An increase in the shear rate was found to cause a decrease in the apparent viscosity of the polymer under test: a doubling of the shear rate reduced by one third the apparent viscosity of most commonly used SDP materials.

A power law expression has proved a reliable means to characterise the changing viscosity of a polymer with differing rates of shear, and such an expression has been used in the calculation of the flow index (n) for the materials extruded from experimental systems.

During vigorous spatulation the apparent viscosity of an SDP material can be reduced by pseudoplastic flow.
When placed in the mouth the combination of temperature rise, plus the reduction in shear rate due to cessation of spatulation, results in a `snap-set' effect.

Barrelling may be seen during any practical demonstration of the compliance of a soft material. If a material is allowed to `barrel' during the compressive phase of a test it will both appear to be and also react as a softer or more compliant material than if it were not permitted to barrel.

Observed compressive dimensional changes are the sum of two separate effects: direct compression at the centre of the speciment and radial displacement at the periphery. For specimens of less than 5mm thick base effects greatly modify the apparent elastic modulus of such polymers. Viscoelastic fluids constrained by a yielding membrane (the epithelial surface) and acting in a non-newtonian manner will demonstrate pressures at the centre of the loaded area greater than at the periphery. Over a protruberance or ridge central pressures may double mean load values.

Conclusions:

The cushioning effect of SDP materials is proportional to:

1. the modulus of the lining applied.
2. the morphology of the ridge,
3. the degree of tissue lubrication,
4. the depth of the soft material.
5. the viscosity of the soft material.

It would appear that classical elastic theory is of doubtful value for the theoretical appraisal of soft liners within the oral cavity; and that existing simple models can only approximately indicate the acceptance and behaviour of SDP materials in clinical use.

CLINICAL USE OF COMPOSITE RESINS IN DENTISTRY. Martin J. Tyas, Director, Australian Dental Standards Laboratory, Australian Department of Community Services and Health, Melbourne, Victoria.

Unfilled polymethylmethacrylate enjoyed brief popularity as a tooth coloured filling material in the early 1960s. There were, however, marked disadvantages resulting from high polymerization shrinkage, material toxicity and colour instability. The development of a specialised dimethacrylate (BIS-GMA) and the ability to incorporate filler, led to the commercial introduction of filled resins for dental use. These early materials suffered from excessive wear in high stress areas, and were colour unstable as a result of the amine catalyst system. Subsequent developments have included higher filler loadings with consequent improved wear properties, and the advent of photopolymerizing catalyst systems with an improvement in colour stability.

Currently available highly filled composites show excellent performance in anterior teeth, however, there are still concerns about their use in posterior teeth. Some formulations, particularly those which are self-cured, can show high wear rates, and the microfine filled products (containing 0.04um dia pyrolytic silica filler) are brittle and prone to fracture. Since the size of a restoration in a posterior tooth is usually larger than that in an anterior tooth, the effects of polymerization shrinkage are more severe. There are no reliable laboratory tests which will predict clinical wear, and the long term clinical trials which are therefore necessary mean that assessment of new products is slow.

The restoration/cavity margin is the area which is most vulnerable to failure, because of the potential existence of a micron size gap resulting from 6-8MPa stress of polymerization shrinkage and into which bacteria and oral fluids can penetrate. This results in staining around the margins of the restoration with loss of aesthetics, the possibility of further caries, and damage to the pulp. Ideally, therefore, the restorative material should bond chemically and/or mechanically to the tooth in order to prevent the gap forming. The tooth consists

of four main structures; enamel, dentine, pulp and cementum, and most restorations are in contact with enamel (98 per cent hydroxyapatite), and dentine (45 per cent hydroxyapatite, 30 per cent collagen and 25 per cent water). Dentine is also a porous structure and readily becomes covered by fluid arising from the pulp. Fortunately, the microscopic structure of enamel makes it amenable to acid treatment resulting in a high energy porous surface into which composite resin can penetrate and bond mechanically. Dentine, however, is not suitable for mechanical bonding, and its surface energy and heterogeneous physical and chemical structure makes it a difficult tissue to which to bond chemically. Over the last five years, unfilled dentine 'primers' have become available, often consisting of phosphate esters of BIS-GMA, which are thought to bond to calcium ions in hydroxyapatite. The tensile bond strength of these primers even under ideal laboratory conditions is usually less than the polymerization shrinkage stress of the composite. There are, however, some promising new materials which offer a better possibility of chemical bonding, either by attachment to dentine collagen, by penetrating and polymerizing in the surface dentine layer, or by binding metal ions on to the dentine surface.

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CARBON/GRAPHITE FIBER REINFORCED POLY(METHYL METHACRYLATE). Karl Ekstrand, College of Dentistry, Univ. of Iowa, Iowa City, Iowa, U.S.A. and NIOM - Scandinavian Institute of Dental Materials, Haslum, Norway and I.E. Ruyter, NIOM - Scandinavian Institute of Dental Materials, P.O.B. 70, N-1344 Haslum, Norway.

Osseointegrated titanium implants of the Brånemark type have been used since 1965 with good clinical results (1). The standard procedure used to fabricate an implant bridge prosthesis is to cast a gold alloy framework and attach polymer teeth. The materials involved are expensive, and the process is time-consuming. Various alternative methods have been proposed.

We have investigated carbon/graphite (C/G) reinforced poly(methyl methacrylate) (PMMA) as a potential material for bridge frameworks. Titanium cones were used for fixation of the C/G reinforced PMMA bridges to the implants. Bonding PMMA to titanium with a silanization procedure might improve the attachment of the cones to the bridge.

The aim of this study was to evaluate various material properties and the practical use of C/G reinforced PMMA for implant fixed bridges.

Test specimens of C/G-PMMA composites for transverse bend testing were stored either dry at 37°C for 30 days or in distilled water at 37°C for up to 90 d. Both unidirectional and braided tubular C/G fibers were used. When specimens with unidirectional fibers were tested in the dry condition, the flexural properties increased markedly with increasing content of fibers in the polymer. However, storage in water at 37°C for up to 90 d led to a significant decrease in the flexural properties. When the flexural properties of C/G-PMMA composites with cleaned, or cleaned and sized fibers were tested, only small differences in flexural behavior were recorded between dry and wet storage conditions (2,3).

Silanes may be used as adhesion promotors between metals and organic polymers. Investigations to determine the flexural properties of heat-polymerized PMMA bonded to silane treated polished titanium were performed. The bond strength of silanized titanium joined to PMMA was measured in 4-point bending after storage in air and water. The average bond strength after dry storage was 25 MPa. Water storage for up to 90 d reduced the bond strength by 50% (4).

Forty patients were selected for the clinical evaluation. All inserted implants were of the Brånemark type. Various fixtures and abutment lengths were used in different situations, depending on the anatomic prerequisites. The fabrication of a C/G reinforced bridge was performed on a gypsum mold of the jaws. Titanium cones were fixed to the abutment replicas with gold screws. C/G fibers were placed around the cones and embedded in the polymer. Polymer teeth were attached, and final coatings of an opaque and a pink polymer covered the exposed areas of the black composite.

The observation times varied from 1 year and 2 months up to 5.5 years. With the exception of 2 bridges, all are functioning. In 2 bridges fractures propagated along the interface of the distally placed titanium cone and polymer. The registered fractures were due to a reduced quantity of fiber loading in the fractured area. Otherwise, no technical complications have been recorded (5,6).

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DENTAL RESTORATIVE MATERIALS - STRUCTURE AND PROPERTIES.

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Prior to the 1960s, most of the restorative and prosthetic materials were inorganic salts, ceramics or metal alloys which were unstable, incompatible with the existing dentition or had poor aesthetics. Today, photo-polymerized resins, inorganic/organic hybrid polymers, fast curing elastomers and dentine adhesives have allowed the conservation of the natural dentition, the design of accurately fitting prostheses and have provided truly aesthetic dentistry. The major developments have been in the area of restorative materials which will be discussed in this lecture.

Dimethacrylate based composite resins were first introduced in 1958 to provide a substitute for the water sensitive silicate cements [1]. These dimethacrylate composites basically consist of a silane-coated glass (originally crushed quartz) dispersed in a blend of dimethacrylates (such as bisGMA and TEGDMA. A wide range of reinforcing fillers has since been commercially utilized, including sub-micron pyrolytic silica, radio-opaque glasses, hybrid organic/inorganic (or splinter) particles and partially stabilized zirconia. Experimental systems have investigated the value of porous particles, short fibres and sintered glass as reinforcement systems.

The di- (and tri-) methacrylates used commercially are based on either an aromatic or aliphatic backbone with ester, ether or urethane linkages. Variations in the water absorption, polymerization shrinkage and surface energy characteristics have also been introduced with fluorinated, spiro-orthocarbonates or siloxane-based backbones. However most research has concentrated on the polymerization process which transforms the material from a viscous paste to a rigid glass. This transition is controlled by the kinetics of the initiation, inhibition and propagation steps in the free-radical polymerization. As shown by rheological measurements, the nature of the inhibitor plays a vital role in providing a working time prior to the onset of curing for the two component, self-cured resins. The more recently developed photo-cured materials contain an α-diketone/2^0 amine redox couple which is initiated by 470 nm radiation. These materials have an unlimited working time but suffer a lack of polymerization in deep restorations due to the preponderance of inhibitor over free radicals.

As a result of the 37^0C cure temperature, high levels of residual methacrylate unsaturation remain in well-cured composites. This has long been con-

sidered detrimental to their properties however firm evidence has been lacking. Recent work [2] has now shown that the presence of unreacted dimethacrylate sol species exerts a significant lowering of the fracture resistance via a plasticizing mechanism.

In many situations, a more biocompatible restorative is provided by the polyelectrolyte based materials. The original development in this area involved the reaction of a concentrated poly(acrylic acid) solution with a heat-treated zinc oxide powder, thus forming a cation-crosslinked network [3].

This material has now been largely replaced by the glass ionomer restorative. Here the crosslinking cations are supplied by an ion leachable calcium fluoro-alumino silicate glass and an acrylic-itaconic acid copolymer is preferred to the homopolymer. Spectroscopic and rheological studies reveal that although the rate of ionization of the carboxylic acid groups is slower than in the zinc polyacrylates, the gelation process is more abrupt [4] due to the combined influence of the more stable complex formed with the aluminium cations and the presence of a chelating agent (tartaric acid).

Selective degradation of the matrix shows that the setting process is not terminated by the formation of a polymeric glass and continues for several months [5]. This behaviour correlates well with the observed improvement in mechanical properties as the material ages.

By comparison with composite resins, glass ionomers are rather brittle, having a lower fracture toughness and larger inherent flaw size. In part, this may be attributed to the low polymeric content in the matrix phase of glass ionomers and to the incorporation of voids during the mixing stage. However, the minimal shrinkage during cure and the ability to chemically adhere to the dentition makes these polyelectrolyte materials worthy of further development.

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PROTEIN ADSORPTION ON POLYURETHANE BIOMATERIALS: The Role of Vitronectin in Blood-Surface Interactions

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INTRODUCTION The study of protein adsorption to solid-liquid interfaces is important for the understanding of several phenomena such as drug delivery, receptor-ligand interactions and artificial surface induced thrombosis. It has been demonstrated that the adsorption of proteins to polymers upon blood exposure is an event of primary importance in determining subsequent thromboembolic events [1]. Thrombosis induced by nonporous microscopically smooth, polymer surfaces involves a series of events beginning with the deposition of protein layer at the blood polymer interface [2]. The formation of this protein layer is followed by the adherence of platelets, fibrin, and possibly leukocytes [3]. Further deposition with possible concurrent entrapment of erythrocytes and other formed blood elements in a fibrin network constitutes thrombus formation. The growth of this thrombus eventually results in partial or total blockage of the lumen of the polymer tubing if the thrombus is not sheared off or otherwise released from the surface as an embolus [4].

In the area of protein adsorption to biomaterials, vitronectin (VN) is of interest because of its role in cell adhesion and spreading, in coagulation and in complement activation, three important aspects of artificial surface

induced thrombosis.

Vitronectin is a single polypeptide glycoprotein found in plasma at a concentration of about 250 ug/ml [5,6]. Vitronectin exists in two biologically active forms, a 75kd and a 65kd polypeptide. VN is has also been identified as the "S" protein of the complement pathway [5]. Both VN and fibronectin (FN) contain the RGD tripeptide sequence which binds to cell receptors, however, VN accounts for most of the cell adhesion and spreading activity of serum [5]. In the complement pathway, VN binds to the hydrophobic region of the C5b-7 complex [7], preventing adsorption to and lysis of cell membranes, and functions as a regulator of C9 polymerization [8]. VN is also involved in the coagulation pathway. It binds to the thrombin-antithrombin III complex which inhibits the inactivation of thrombin by antithrombin III thus countering the action of heparin.

EXPERIMENTAL Human VN was isolated and purified by the method of Dahlback and Podack [7]. An FTIR/ATR spectrum of VN was obtained on a Mattson Serius FTIR with a Circle Cell. Adsorption kinetics from 0.01 and 0.03 mg/ml solutions in phosphate buffered saline (pH 7.4) are measured from non-flowing solutions using a FTIR/ATR flow cell as described previously [9].

A circular dichroism spectrum of VN was obtained on a Jasco 20-A spectropolarimeter.

RESULTS Previous studies have shown that in general, the adsorption of blood proteins is dependent upon the surface-water interfacial energy, with a general trend that adsorption increases as interfacial energy increases. In this situation, protein adsorption may be thermodynamically driven by the reduction the surface-water interfacial energy which occurs as the protein adsorbs. This trend has been observed for albumin and fibrinogen, and for fibronectin.

We have determined the adsorption of vitronectin to a number of polymer surfaces *in vitro*. Compared to adsorption data describing other globular blood proteins such as albumin or fibronectin, vitronectin adsorbs more avidly to polymers. Further studies done utilizing Fourier Transform Infrared Spectroscopy with Attenuated Total Reflectance (FTIR/ATR) and circular dichroism spectra indicate that vitronectin adsorption to polymer surfaces may be independent of surface interfacial energy, and that conformational changes in the molecule occur upon adsorption.

Characterization of vitronectin with respect to diffusivity and sedimentation indicate that it may serve as a primary mediator of artificial surface induced thrombosis. Further studies to evaluate the affects of adsorbed vitronectin on acute thrombus deposition and embolization have been carried out utilizing a variety of polymer surfaces in our canine *ex vivo* series shunt model.

Our data indicates that preadsorbed vitronectin stimulates thrombosis and related phenomena. Vitronectin has been shown to be initially as thrombogenic as fibrinogen or fibronectin on similar polymer surfaces. However, maxima obtained on vitronectin preadsorbed synthetics occurred at much shorter blood contact times. Further studies to evaluate the significance of this temporal disparity between vitronectin and other glycoproteins are currently underway.

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FAILURE OF VASCULAR GRAFTS: CORRELATION WITH STRUCTURE AND MATERIAL PROPERTIES

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With the widespread use of synthetic arterial grafts, complications inherent to these prostheses are being reported and it must be noted that the true incidence of failure of arterial grafts is believed to be significantly greater than that reported in the literature [1]. So far not sufficient emphasis has been placed on identifying those inherent features of the vascular grafts that could contribute to their long-term success or short-term failure.

In the present study a critical review of the structural and material factors contributing to the mechanical breakdown of arteries and artery/implant composite systems is proposed, based on a recent review article [2]. A brief explanation of the type of materials and textile structures used in vascular grafts is presented. The most important causes of graft failure are underlined as well as the time to failure and relative frequency of each failure mechanism. This is performed by means of the Weibull failure probability model [3], which is applied to vascular graft failure data reported over a period of 30 years. The main objective of this analysis is to attempt to separate out the various modes of failure of vascular grafts occuring at various times under physiological stresses using statistical tools. The trends observed in graft failure are clear and can be summarized as follows. Four major causes of failure of medium to large size artery/implant systems are observed: (a) Dilatation, the most frequent failure mechanism, occurs early and/or late in the graft life span, and is brought about by the rearrangement of the textile structure of the graft, and/or by yarn fatigue under the action of the physiological pressure. (b) Suture line failure is the next

major cause of failure and occurs mostly between 30 and 50 months of implantation. It is caused by compliance mismatch between graft and artery, or by failure of the suture material itself. (c) Failure due to handling or manufacturing defects is the next cause of failure. It is less common and arises after 40-60 months of implantation. (d) Bleeding and infection is the earliest, and the rarest cause of failure, mainly within the first ten months following implantation.

Future research areas important for characterizing the mechanical behaviour of artery/implant systems are suggested, with the aim of establishing rational standards for prosthesis evaluation.

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THE EFFECT OF ALBUMIN COATING ON THE IN VITRO BLOOD COMPATIBILITY OF DACRON ARTERIAL PROSTHESES

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Introduction

Knitted Dacron has been used as an arterial vascular prosthesis in the replacement of large- and medium-sized arteries, primarily because its porosity promotes graft healing, even though Dacron is recognized to be highly thrombogenic[1]. However, the high porosity of the graft also makes it mandatory to preclot the prosthesis in order to prevent hemorrhage through graft interstices after implantation. This preclotting procedure leads to a flow surface which is highly thrombogenic[1]. Compound Dacron prostheses with a crosslinked albumin surface, developed to produce a prosthesis which did not need to be preclotted[2] have shown improved patency while still allowing tissue ingrowth and healing[2]. However, little quantitative work has been done with respect to the effect of the albumin coating on the thrombogenicity of these prostheses. This study was carried out to investigate the effect of albumin coating on the graft interaction with platelets, leukocytes and coagulation factors.

Methods

The work described here utilized a recirculating, in vitro perfusion system[1] containing fresh human donor blood, to assess quantitatively the effect of crosslinked albumin precoating on the thrombogenicity of Dacron. The evaluation involved a comprehensive analysis of platelet activation, encompassing platelet count, release, aggregation, and platelet adhesion. Fibrin formation was assessed by measuring fibrinogen levels and fibrinopeptide A production; leukocyte interaction was analyzed by measuring total leukocyte concentation, and cell adhesion to the graft surface was assessed by scanning electron microscopy. The albumin coating provided a film-like covering for the Dacron with little change to the graft

topography, although the coating appeared brittle.

Results and Discussion

The results of all the in vitro characterization methods showed that the albumin coating significantly improved the short-term blood compatibility of Dacron. The platelet count in the circulating blood decreased with perfusion time for Dacron until by 30 minutes, it had declined to 69%±2% of baseline; while the platelet count for albumin-coated Dacron did not change significantly from baseline. Platelet release of platelet factor 4 and β-thromboglobulin, by 180 minutes, for Dacron were 38±30 times and 70±18 times baseline respectively; while the albumin-coated graft caused significantly less ($p<0.03$) platelet release. In addition, the albumin coating diminished coagulation activation and fibrinopeptide A formation compared with the uncoated graft. The total leukocyte concentration in the circulating blood decreased significantly for Dacron by 180 minutes, while that for albumin-coated Dacron did not change significantly from baseline levels. By SEM, there were numerous leukocytes and platelets adherent to the Dacron graft surface, while deposition was minimal on the albumin-coated surface. However, there was clear evidence from SEM of some flaking of the brittle albumin coating by 180 minutes of perfusion.

The results of this study showed that the albumin coating significantly improved the short-term blood compatibility of Dacron. This does not necessarily make the modified prosthesis superior to uncoated Dacron, because of the potential long-term problems associated with flaking and peeling of the crosslinked albumin coating. However, this study does confirm the findings of others[3] which suggest that thrombogenicity is not solely determined by surface morphology, but is also strongly influenced by surface composition.

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THE TENSILE PROPERTIES OF VASCULAR PROSTHESES

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ABSTRACT A difference in compliance between the graft and the natural artery will cause stress at the point where they are sutured together and failure may result. The compliance and fracture loads of the graft was examined by means of longitudinal tensile tests.

The properties of the meshes, used to manufacture artificial arteries, were consistent. The collagen in the vascular graft failed at a variety of loads which were all well above the natural artery strength. This test method may be used to determine the thickness and quality of collagen on the graft.

1. INTRODUCTION

Vascular prostheses have proven beneficial in alleviating distal blood flow impairment by replacement of blood vessels either in, for example, the lower trunk or limbs. The prosthesis may be manufactured by a variety of techniques (1,2). The long saphenous vein continues to be the graft of choice for arterial substitution in arteries below 6 mm in diameter. The biosynthetic prostheses manufactured under the trade name 'Omniflow' uniquely combine the properties of a synthetic mesh with those of tanned biological tissue.

2. MATERIALS

A brief description of the manufacturing process for the Omniflow vascular graft follows. Initially a cylindrical tube of knitted dacron mesh which will form the basic structure of the graft, is placed over a silicon mandrel. The mesh covered

mandrels are then implanted into the dorsal subcutaneous tissue of anaesthetized adult sheep. The entire implant is removed after 12 to 14 weeks and trimmed of excess subcutaneous fat and then placed in a glutaraldehyde tanning solution.

A variety of knitted dacron meshes may be used and the meshes used in the present study are designated as Cap II and Cap III. These meshes both have the same type of knitted structure but different yarns are used in their manufacture. Cap II is made from relatively thin straight fibres of 44 denier; whereas Cap III meshes are constructed from thicker, 136 denier fibres that are 'wavy' or 'kinked' due to "texturing".

3. THE TENSILE TESTING OF VASCULAR GRAFTS

The compliance (3-5) of the graft was examined by means of longitudinal tensile tests. Both knitted dacron mesh alone and the mesh reinforced with collagen were tested. The fracture loads and the compliance (extension divided by the force) were measured for both types of materials. The tensile testing arrangement and procedure was not routine. Specially designed grips in the shape of a cylinder enabled the mesh or graft to be secured. The tip of each grip was rounded to minimise stress concentrations due to a reduction in the sample diameter under stress.

4. RESULTS AND DISCUSSION

Under tension the arterial graft showed a graph exhibiting two fracture points; one that can be attributed to the collagen failing and the other to the failure of the dacron mesh. The arterial graft is about twice as stiff as the dacron mesh and fails at about 27% strain. The load drops rapidly after the collagen fails to a mid-range value while the mesh tears away from the collagen. The mesh itself then comes under direct tension and fails in a manner characteristic of the mesh type. It is really only the first fracture point that is of major interest because after the collagen fails the artificial artery ceases to function.

The collagen supports the majority of the load in the region prior to the coll-

agen failure since it is the stiffer component. The mesh maintains the dimensional stability of the composite. The mesh can only support a significant part of the load after the collagen fails. However the mesh still plays an important part in the structure of the prosthesis. The Cap III is a heavier yarn resulting in a thicker collagen coating. The nature of the collagen laid down and its biological performance is under investigation.

5. CONCLUSIONS

1. The method established for the longitudinal tensile testing of arterial grafts and dacron meshes is consistent and reliable.

2. The Cap III mesh material has a higher failure load and greater elongation at failure than the Cap II mesh. Despite this the compliance or stiffness of the two meshes is almost the same.

3. While the properties of the meshes used to manufacture artificial arteries were consistent, the collagen in the graft failed at a variety of loads, all well above natural artery strength.

4. There are possible applications of this method of testing to determine the thickness and quality of collagen on the graft.

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Polymer Composites for Orthopaedic Implants

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The use of metallic implants for the treatment of bone fractures can lead to a non-physiological situation in which the healing bone is protected from normal loading levels. In a rigid fixation the healing pattern is different from that seen in fractures treated by plastic since the absence of movement at the fracture site suppresses one of the modes of healing.

These considerations have led to an interest in alternative systems of fixation which should generally be more adapted to mechanical and biological requirements of bone healing. Polymer fibre composites are of interest because they combine high strength, good fatigue properties, an elastic modulus lower than metals and the absence of metal corrosion products. The reduced modulus means that more of the applied load can be carried by the bone in the new bone-fixation system produced by the surgeon and the lower rigidity attainable can assist healing processes. Since a fully elastic (recoverable) deformation is shown by these composites a stable fixation is obtained which retains the anatomical alignment of the bone fragments but allows some controllable extent of movement. The fatigue properties of the composites mean that the device does not have to be protected in the same way as a metal plate to avoid failure by breakage and thus patients can be allowed a full level of normal activity. This retains muscle tone, joint mobility and provides the stressing of the fracture to promote healing.

The materials now being used are made from high strength carbon fibre epoxy resin prepreg which is heat laminated under pressure using 0^{o},$+45^{o}$ &-45^{o} fibre alignments. Holes for screw attachment to bone are machined into the plates after resin curing is complete. The first clinical series for treatment of tibial fractures has been reported (1) and demonstrated the mechanical advantage of the plates not so much in terms of lower stiffness, which is dependent as much on dimensions as on materials properties, but with regard to the ability to produce a stable fixation which could permit weight bearing

without fear of fatigue failure. Early fracture consolidation by callus bridging the gap was seen. A recent series in the forearm has been completed (2, 3) and as in the tibial series stainless steel screws were used for attachment. Good clinical response has been observed in over 30 patients and the work is continuing using titanium screws. A brief report has been made (4) concerning a new attachment method with composite expandable pins.

The use of these composite materials has been extended to use as anterior spinal implants and the horseshoe shaped implants are generally used in conjunction with bone graft or in the future with hydroxyapatite.

A range of in vitro and in vivo tests showed the biocompatibility of the material for these orthopaedic applications. Clinically new bone sometimes incorporates the implant and an investigation is under way to try to explain this in terms of the properties of fibre or composite. Carbon fibre has an electronic structure that gives it diamagnetic properties.

By means of newly developed equipment the piezo-electric nature of the composites has been shown and the clinical significance of this is being studied.

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SELECTION OF POLYMERIC MATERIALS FOR COSMETIC HAND PROSTHESIS

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ABSTRACT

Orthopaedic requirements have grown remarkably over the last few years. Loss of arms, hands or fingers due to diseases and accidents have become more frequent. With the quality of life being improved continuously, the physiological expectations of patient, who have lose their hands or fingers have also been raised to a level where they no longer are satisfied with iron hands or wooden unaesthetic prosthesis. The age of polymers which started in the early 1930s have resulted in many new prosthetic designs. Among the many designs is the cosmetic hand prosthesis which looks like real hand in terms of shape, colour, texture and other physical appearances. The advantages of polymers in cosmetic hands prosthesis are that they can be coloured easily, soft, durable and easily molded into shape. However not all polymers can be used. Requirements such as good replication properties, permanence of colour, resistance to staining and fungus growth, durable over a wide temperature range and low toxicity need to be considered. This paper describes the materials selection procedure of polymeric materials ranging from silicone base polymers to polyvinyl chloride for making the cosmetic hand prosthesis. The procedure involved in the derivation of weighting factors and material performance index in order to arrive at an objective decision with regard to the final choice of the material is made. Discussion of the material properties of various suitable polymers and projection of future trends are also made in this paper.

1. INTRODUCTION

Historical records have shown that human, in search for a better quality of life, have sought various kinds of substitution for missing or amputated limbs such as the hand, arm and leg which may be the result of accidents, diseases or birth defects. This artificial substitute part is known as a prosthesis. As science and technology progresses with new materials, new inventions and new manufacturing technique, these artificial substituted parts not only function well but also look real.

The first recorded use of a prosthetic hand was the artificial hand used by Marcus Sergius, a Roman general who lost his right hand in the second Punic War (218 - 201 B.C.) and was subsequently fitted with an iron hand [1]. It was reported that he then continued to participate in the battles. Earlier iron or wood prosthetic hands were crude. However, since 1886 where a heavy-duty hand was developed, improvements were made. By 1904, a versatile prosthesis for the upper amputee was produced.

Many of these prostheses, though functional, do not look real. They are not aesthetic. This gave a great psychological set back to patients who very often hide their artificial hand by wearing gloves. As the expectation of patient increases, modern hand prosthesis took a new turn. They begin to look like the real hand in terms of colour, texture and overall appearance. In fact some of them were so good that it is difficult to distinguish the real one from the artificial one. The hand prosthesis can now offer true psychological therapy, functional and rehabilitation advantages to the amputee [2]. All this was the result of the development of the cosmetic hand glove. It is this glove that replaces the ordinary gloves that once hide the crude looking artificial hands.

Cosmetic hand prosthesis came about with the advent of new polymeric materials which find rapid commercial use since 1930. The main advantages of these materials are that they can be coloured easily, have mechanical properties similar to that of the human skin, are weather resistant and can be moulded easily. The cosmetic glove can be described as a plastic glove that resembles the human hand skin in texture, shape, colour and other natural skin details.

2. THE HUMAN SKIN

Before one can fully emulate the properties (may it be the appearance or mechanical strength) of the hand so as to produce a cosmetic glove, one needs to study the structure of the human skin.

The human skin is the largest organ in the body whether it is by weight or by volume. Its main function is to protect the body in a wide variety of ways. It is almost waterproof and hence prevents the

escape of body fluids and at the same time permeable to water vapour and gases. It also protects the body from harmful bacteria and chemicals. The skin protects underlying tissues from harmful rays such as ultra violet light from the sun. In addition, the skin has many nerve endings that are sensitive to cold and heat as well as pressure, touch and pain.

Basically the skin has three layers: (1) epidermis, (2) dermis and (3) subcutaneous tissue (see Fig. 1). The epidermis, the outermost layer, is about 0.5 to 1.5 mm thick. The dermis, the middle layer is about 15 to 40 times as thick as the epidermis. The subcutaneous tissue, the innermost layer, varies greatly in thickness in different parts of the body.

The epidermis itself is composed of four layers of cells, namely the horny, granular, spinous and basal layers. They are approximately 15 to 40 rows of dying cells in the horny layer which is translucent in colour. These cells are tough and waterproof. They are filled with a protein called keratin. The granular layer has one to two rows of dying cells which contain small grains of substance called keratohyaline. The spinous layer is composed of about 4 to 10 rows of living cells. The basal layer is also composed of living cells. It is here that the melanocytes cells are located. These cells produce a brown pigment called melanin the amount of which determines the skin colour of many individuals. For example, dark skin is the result of an abundance of melanin when compared to a light skin. The amount of melanin produced in each person's skin is determined mainly by heredity. Nevertheless, exposure to sunlight can increase the production of melanin, causing light skin to tan. The basal layer also contains the hair, nails and glands.

The dermis is made up mainly of connective tissue, blood vessels, and nerve endings. The subcutaneous tissue has in addition to the dermis, fatty cells. It is the subcutaneous layer that protect the body from blows and knocks.

From the above description, it can be seen that the skin has many complex layers with different properties. The structure-function relationships of skin may give guidance as to how cosmetic hand gloves can be made especially in the selection of proper polymeric materials.

3. REQUIREMENTS OF A COSMETIC HAND GLOVE MATERIAL

The success or failure of any prosthesis is judged on the basis of acceptance or rejection by a patient, which for a cosmetic hand glove depends largely on the aesthetic effect of the glove.

The main function of the cosmetic hand glove, apart from the aesthetic function, is also to act as an outer cover for a hand with missing fingers or for a complete mechanical prosthetic hand. Because

it is an outer cover, its properties should be similar to the epidermis of the human skin so that it will be pychologically acceptable to the patient. However, the epidermis is a living tissue, capable of undergoing repair whilst the cosmetic hand glove is a synthetic material once worn cannot be repaired by itself. The cosmetic hand glove material will therefore need extra properties which will overcome their non-self repairable state.

In order to aid materials selection, eleven properties are deemed most important. They are: (1) replication, (2) colour permanence, (3) staining, (4) abrasion resistance, (5) toxicity, (6) flexibility, (7) durability, (8) chemical inertness, (9) washability, (10) permeability and, last but not the least, (10) cost.

1) Replication

Because aesthetic aspects are very critical in the ultimate evaluation of whether success or failure for a cosmetic hand glove, good replication properties of the polymeric material is essential. This property ensures that the textural features of the hand are faithfully reproduced. However there is no standard in measuring replication properties of materials. It is generally accepted that this is very much related to the shrinkage of the material after permanent set (whether by crosslinking in the case of thermosets and elastomers or cooling in the case of thermoplastics) has occurred. The lower the shrinkage the better the replication properties. The viscosity of the polymeric resin also plays an important role in the replication properties. This is because in order to reproduce a textural feature the resin must flow easily over the feature and cover the feature completely with as little as possible of trapped air bubbles. The lower the viscosity before permanent set the better will be the replication properties. For thermosetting materials the viscosity of the resin and the hardener need to be evaluated. For thermoplastic materials which soften on heating the viscosity-temperature and viscosity-shear rate profile needs to be studied carefully.

2) Colour Permanence

Aesthetic qualities should be permanent as far as possible. The colour that comes out of the manufacturing workshop must remain the same under normal exposure to light. This property is often controlled by the additives added in the polymeric resin and the choice of colour pigments. However some polymers such as the acrylics do not change significantly in colour and are excellent in outdoor applications. The reason why acrylics are good in colour permanence is because the absorbed ultra violet light have very little chance to participate in chain breaking there by causing the material to degrade and change colour. The colour permanence is therefore closely related to the chemical structure of the polymer.

3) Staining

Since the cosmetic hand gloves are always in contact with food, newspaper prints, coffee, ink, etc. good resistant to staining is essential. The staining properties are related to the surface roughness, surface energy, surface diffusivity and chemical structure of the polymer. Generally chemically inert material such as silicone rubber and teflon are excellent in stain resistance. The lower the surface energy the better the stain resistance.

4) Abrasion resistance

Since the cosmetic hand glove cannot undergo self repair, it must have good abrasion resistance, otherwise all the textures on the surface will wear out easily. This property increases with hardness and is dependent on the morphological structure of the polymer.

5) Toxicity

This property is perhaps the most important where human lives are concern. It is through the hand that many elements (toxic and non-toxic) enter the body. The majority of the toxic elements comes from the additives, fillers, processing aids, lubricants, heat stabilisers and antioxidants that are incorporated in the polymer during fabrication and/or during compounding. The lesser additives added the lower the toxicity of the polymer. Often these additives, such as the amines and chromates, can cause severe dermatitis.

6) Flexibility

The cosmetic hand glove primary function is to act like a glove which undergoes high degree of flexion. For this reason, only elastomers are the only choice since they have high elongation to failure.

7) Durability

The cosmetic hand glove will be exposed to all kinds of weather. A good cosmetic hand glove material must have good weathering resistance, good mechanical properties over a wide temperature range, fungus resistance and fatigue resistance - all of which are related to durability property of the material.

8) Chemical Inertness

Like toxicity this is an important property. However it is not so much related to the additives of the polymers but to the chemical structure of the polymer and its response to solvents. Some of the solvents can cause environmental stress cracking.

9) Washability

All cosmetic gloves will get dirty over some period of time. Generally a material that has good stain resistance has good washability property. However the washability of the material is more related directly to the removal of dirt or stains by normal washing in water or light detergent or light solvent. In other words a material that will not dissolve, swell or deteriorate in water or light detergent is most useful.

10) Permeability

One of the greatest problem with many artificial limbs is the accumulation of perspiration which not only cause prosthetic loosening but also infection. In the case for the cosmetic hand glove, high permeability is desirable as it allows water vapour to escape from the underlying skin and also to allow some exchange of gases which may be vital to promote healthy growth of the skin.

11) Cost

A cosmetic hand glove at the present moment cost a lot and is beyond the means of many patients, especially when they realised that the glove gets worn out like our shoe and need to be replaced frequently (on the average once in six to nine months). The total cost can basically be divided into material cost and fabrication cost. The lower the cost the more desirable.

4. POLYMERIC MATERIALS FOR COSMETIC HAND GLOVE

Many polymeric materials have been tried ranging from natural rubber to the vinyl chloride plastics [3]. The earliest material for glove was leather which is soft and has high tear strength. But it suffered from its low extensibility, washability and colour properties. Natural rubber was used as an ideal choice in the 1940s [4] when other elastomers were not so well known. However the extreme shrinkage of rubber, its inferior aging properties which leads to discoloration and its inherently poor oil resistance rendered it unattractive for glove material. Chemicals such as antioxidants can be used to prevent aging, but the effective ones darken the film. The unsaturated double bonds make the rubber very susceptible to oxygen and ozone attack which eventually lead to cracking.

Synthetic rubbers (copolymers of butadiene styrene and acrylonitrile) were also tried but they have similar problems to that of natural rubber. The acrylonitrile rubbers have good resistance to grease, oil and many solvents, but the additives required to develop strength, chemical resistance and so on have a general tendency to whiten the rubber when stretched. As a result, synthetic rubbers are mainly used as industrial gloves.

With the advent of large commercial production of polyvinyl chloride (PVC) as early as 1950s and the realization that PVC can be plasticized to form a variety of soft plastics [5], many cosmetic gloves were made of this material. When properly compounded, PVC yields tough and flexible films with good resistance to chemicals and aging properties. Infact, as early as 1947, both the Mellon Institute for Industrial Research and the Army Prosthesis Research Laboratory in U.S.A. [3] selected this material as the most promising for the production of cosmetic gloves. However, with real life tests it

was realised that PVC stains easily and is less flexible at low temperatures which means that different cosmetic gloves need to be worn for different seasons (one for summer and one for winter). The replication properties and their tear strength of PVC are also relatively poor. On exposure to ultraviolet light over a period of time, it hardens, thus reducing its elasticity. Various formulation were tried to increase the flexibility of PVC by changing the plasticizer to filler ratios. However the results was a decrease in durability of the glove and some of the additives such as lead and cadmium compounds which are used as stabilizers are toxic and pose a problem of health hazard. Other additives when added in large amount can cause contact allergy.

Realizing the importance of high tear strength and good fatigue endurance properties, other materials were sorted, and polyurethane was selected. Polyurethane has also good non-toxic properties and bio-compatibility. As a result, it finds use in implant devices such as those in heart-valves components [6]. However it lacks in flexibility and has poor colour permanence making it unsuitable for cosmetic hand prosthesis and generally tend to loose out to PVC in this application [7].

It took almost a decade before researchers in this field had to move away from looking at organic polymers for a solution. The best compromise of properties came from inorganic polymers - silicone rubber. Although silicone rubber was first discovered in 1850 [5], it did not receive much attention until the 1970s. It is in space research that opened the door to the potentiability of silicone rubber. The first man on the moon, Neil Armstrong, had the majority of the material used for his space suit which needs to withstand a wide temperature range, be flexible and chemically inert, out of silicone rubber. Furthermore, the low viscosity of the silicone resin allows intricate copying of fine surface texture. It is this good replicating property that makes silicone rubber a promising material for making cosmetic gloves. It can be built up from different tinted layer, producing life-like appearance with inherent non-staining and non-sticking properties [2,8]. The mechanical strength of silicone rubber also resembles that of the natural skin [8]. However it has relatively poor tear strength and fatigue properties. Typical tear-propagation strength of earlier conventional silicone rubber is about 13 kN/m (75 lbs/in) (ASTM D624, DieB). Developments by Dow Corning Corporation has produced high-performance silicone rubber with typical tear-propagation strength of 52.5 kN/m (300 lbs/in) and a significant increase in fatigue properties. However, these values are still not as good as those in polyurethane and most commercial silicone rubber are considered to have poor abrasion, tear and fatigue properties.

5. MATERIALS SELECTION PROCEDURE FOR COSMETIC GLOVES

There appear to be no single material that will satisfy all the requirements for making a good cosmetic glove. A compromise has to be made and an objective materials selection procedure needs to be adapted [9,10].

The first step in this procedure is to determine the weighting factors for each requirement using a digital logic approach where each requirement is compared pair-wise. A "1" is given to the more important property and "0" for the less important one. If both properties are of equal importance a "1" is given for each. The total number of possible comparisons (N) is given by $N = n(n-1)/2$ where n is then calculated by $w_i = m_i/M$ where m_i is the number of positive decisions or scores for each property and M is the total score for all the properties.

The above procedure of determining the weighted property index is shown in Table 1. Interestingly, for clinical reasons, toxicity has the highest weighting factor. For cosmetic and economic reasons, replication properties, colour permanence, resistance to stains and cost are the second highest. As chemical inertness is related indirectly to resistance to stains, it is the third highest followed by durability, the fourth highest. The fifth highest is washability and permeability and, least of all, are resistance to abrasion and flexibility. However it must be pointed out that different weighting factors will be arrived at by different group of people.

Having derived the weighting factors, material performance index which is used as a decision index can be assigned to each possible material for making the cosmetic glove. Table 2 list six possible polymeric materials. Since the properties are not readily expressed numerically, scaled properties [9] are difficult to arrive at. Relative gradings (10 for excellent, 5 for satisfactory and 0 for very poor) are therefore used in substitute for the scaled properties (S_i). The material performance index (P) is defined as

$$P = \Sigma S_i w_i$$

From Table 2, it can be noted that silicone rubber at the present moment appears to be the most suitable compromised material for cosmetic gloves, with polyurethane and polyvinyl chloride (PVC) the second and third best respectively.

6. FUTURE TRENDS

The trend for future development in the choice of material appears to be in blending various polymeric materials together to give enhanced properties from two or more base polymers. For example, Kitayama et. al. [11], made various cosmetic glove materials from a blend involving PVC, silicone rubber and synthetic rubber in the hope of obtaining good resistance to abrasion, improvement in durability and reducing the cost of the material. Some improvements along those areas have been noted and new materials of this nature are constantly being discovered.

The other future trend is in the area of fabrication technology using computer aided design (CAD), computer aided manufacturing (CAM) and computer colour matching so as to reduce cost and speed up the process of production. At the present moment making a cosmetic hand gloves require a donor hand for the patient. The donor hand is used purely for replication purposes so that a mould can be made. The procedure for obtaining a matching donor hand is tedious. Moreover presently, aesthetic effect requires a good artist to paint the plastic glove so that it will look real. Here colour matching is a real problem. The above two process accounts for the high cost and long period of delivery.

If ever the cost and delivery time of cosmetic hand gloves are to be reduced, a multi-disciplinary approach needs to be adopted. This will involve medical staff, materials scientists, mechanical engineers, electrical and electronic engineers, plastic technologists and chemists. Already with the advent of CAD and CAM and related computer aided engineering, developing of a low cost below elbow cosmetic prosthesis is becoming a reality [12,13,14].

7. CONCLUSION

Historical developments have shown that the present state-of-the-art in making cosmetic hand prosthesis has reached a stage of being aesthetically appealing to patients. This has offered a true psychological therapy, functional and rehabilitation advantage to the patients. With the advent of numerous suitable polymeric materials, it is necessary to adopt a more objective method of materials selection for the cosmetic hand glove. The method involving a digital logic approach to determine the weighting factors for each property and employing the materials performance index shows that from the list of candidate materials (natural rubber, styrene-butadie rubber, nitrile rubber, polyurethane, polyvinyl chloride and silicone rubber) silicone base rubbers is the most ideal material for making cosmetic hand

gloves for the present moment. However silicone rubber has poor tear strength and is expensive. Future trends indicate that silicone rubber needs to be blended with other polymers to reduce cost and increase its tear strength. The direction towards the use of CAD and CAM to further reduce delivery time and cost appears to eminent in the 1990s.

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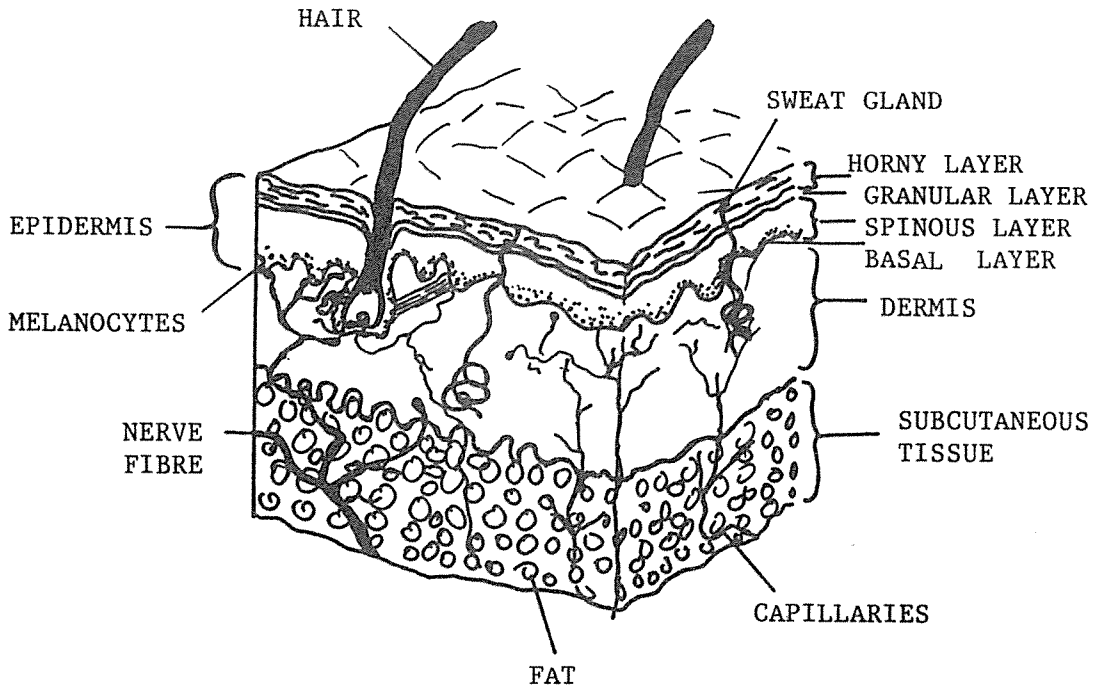

Fig. 1 Schematic diagram showing the structure of a typical human skin

Table 1 Weighted property index for cosmetic gloves selection

Combinations \ Properties	1. Replication properties	2. Colour permanence	3. Resistance to stains	4. Resistance to abrasion	5. Toxicity	6. Flexibility	7. Durability	8. Chemical inertness	9. Washability	10. Permeability	11. Cost	
1 (1:2)	1	1										
2 (1:3)	1		1									
3 (1:4)	1			0								
4 (1:5)	0				1							
5 (1:6)	1					1						
6 (1:7)	1						0					
7 (1:8)	1							1				
8 (1:9)	1								0			
9 (1:10)	1									0		
10 (1:11)	1										1	
11 (2:3)		1	1									
12 (2:4)		1		0								
13 (2:5)		0			1							
14 (2:6)		1				1						
15 (2:7)		1					1					
16 (2:8)		1						0				
17 (2:9)		1							0			
18 (2:10)		1								0		
19 (2:11)		1									1	
20 (3:4)			1	1								
21 (3:5)			0		1							
22 (3:6)			1			0						
23 (3:7)			1				0					
24 (3:8)			1					1				
25 (3:9)			1						0			
26 (3:10)			1							1		
27 (3:11)			1								1	
28 (4:5)				0	1							
29 (4:6)				1		1						
30 (4:7)				1			1					
31 (4:8)				0				1				
32 (4:9)				1					1			
33 (4:10)				0						1		
34 (4:11)				0							1	
35 (5:6)					1	0						
36 (5:7)					1		1					
37 (5:8)					1			1				
38 (5:9)					1				0			
39 (5:10)					1					0		
40 (5:11)					1						0	
41 (6:7)						0	1					
42 (6:8)						0		1				
43 (6:9)						0			1			
44 (6:10)						1				1		
45 (6:11)						0					1	
46 (7:8)							1	1				
47 (7:9)							1		1			
48 (7:10)							1			0		
49 (7:11)							0				1	
50 (8:9)								1	1			
51 (8:10)								1		1		
52 (8:11)								0			1	
53 (9:10)									1	1		
54 (9:11)									0		1	
55 (10:11)										0	1	
M_i	9	9	9	4	10	4	7	8	5	5	9	79
$W_i = \varpi_i / M$	0.110	0.110	0.110	0.055	0.130	0.055	0.090	0.100	0.065	0.065	0.110	1

Total, M

Table 2 Materials Selection of Cosmetic Gloves - Materials Performance Index

MATERIAL / PROPERTY	w_i	1. Replication	2. Colour Permanece	3. Resistance to Stains	4. Resistance to Abrasion	5. Toxicity	6. Flexibility	7. Durability	8. Chemical Inertness	9. Washability	10. Permeability	11. Cost	MATL. PERFORM. INDEX,
		0.110	0.110	0.110	0.055	0.130	0.055	0.090	0.100	0.065	0.065	0.110	
1. Natural Rubber		6	5	5	9	5	7	8	5	6	5	6	6.00
2. Styrene-Butadiene Rubber		6	5	5	8	5	7	7	5	6	5	6	5.74
3. Nitrile Rubber		6	5	7	9	5	7	8	5	6	4	6	6.04
4. Polyurethane		6	5	6	9	9	7	8	5	7	6	5	6.54
5. Polyvinyl Chloride		7	6	5	8	5	8	8	5	6	5	9	6.44
6. Silicone Rubber		10	8	10	5	10	7	5	10	8	9	4	8.04

Grading Scale

10.....	5.....	0
Excellent	Satisfactory	Very Poor

Clinical and Experimental Comparison of Carbon Fibre Reinforced Plastic Plates versus Stainless Steel Dynamic Compression Plates in the Treatment of Fractures.

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A study was performed to compare the effectiveness of Carbon Fibre Reinforced Plastic (CFRP) bone plates with standard Dynamic Compression (DC) plates. A canine fracture model was used, wherein both tibiae were fractured with a "bone-breaker" designed in the authors' Department. This device was essentially a three point bending jig that was instrumented to measure the initial fracture strength of the intact tibiae. The fractures produced by the bone-breaker were consistent and closely resembled real canine fractures.

One tibia of each dog was plated using the standard Association for Osteosynthesis (AO) technique, using a 316L stainless steel DC plate. The other limb was plated with a CFRP plate of similar dimensions, supplied by Johnson and Johnson. These plates had an average stiffness of 0.441 Nm per degree. Fourteen dogs were used, and followed for a maximum of twenty weeks. No postoperative immobilisation was used and the dogs were allowed to move freely in their pens.

Radiographic examination of the healing limbs revealed healing of the CFRP plated tibiae with abundant callus, as contrasted to the total lack of callus on the DC plated tibiae. Remodelling of the fracture callus occurred, as in the healing of a natural fracture, and was almost complete between 10 and 20 weeks. The tibiae were harvested at 12, 16 and 20 weeks after surgery. Following harvesting, both plates were removed and the bones tested to failure in three point bending using an Instron universal testing machine.

There was very little difference between the strength of union of the DC plated and CFRP plated fractures at 12 and 16 weeks. At 20 weeks, although the number of results was too small for statistical confirmation, the CFRP plated tibiae were consistently stronger than the DC plated tibiae. In no case did the recovered strength of the bone exceed 83% of the original strength, as measured by the bone-breaker.

The recovered CFRP plates were also tested in three point bending, and were found to have consistently lower stiffness than when implanted, although again numbers were too small for adequate statistical analysis. On dessication the original stiffness was regained. There was also marked tissue staining around most of the CFRP plates, and there appeared to be dissolution of the resin matrix and delamination on many. Some plates also exhibited permanent plastic deformations acquired in vivo.

A randomised trial of a broader eight hole plate made of the same CFRP material to treat human tibial fractures was begun in 1983. Sadly, this had to be abandoned when the firm manufacturing the plates was taken over and the supply stopped. At that time only 11 CFRP and 10 DC plates had been implanted. These numbers were again insufficient for a statistical comparison, but an analysis of these results indicated that the same healing process occurs in humans as in the experimental dogs. All the plates were removed within one year, and there have been no re-fractures.

These results, although too few to allow definite conclusions to be drawn, are at least promising. Fractures in both experimental dogs and humans have been treated with CFRP bone plates, and have responded well. There are still several problems to be addressed before CFRP plating can enter day to day clinical practice. These include the loss of matrix material, with resultant staining of tissue, and the inability to bend plates conform to the contour of the bone to be fixed. For certain classes of fracture though, there would appear to be a place for CFRP plating.

DIFFUSIVE AND SURFACE PROBLEMS DURING UTILIZATION OF HYDROGELS IN OPHTHAMOLOGY

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INTRODUCTION

A variety of transparent hydrophilic and hydrophobic polymeric materials have been developed in recent years for applications as hard and soft contact lenses (1). In all applications, the polymer film is in contact with the cornea and tear fluid flow between the lens and the eye plays an important role in oxygen permeation. Inadequate supply of oxygen through the lens or the tear fluid may result in undesirable symptoms such as hypoxia and various types of edema (2,3).

Soft contact lenses are made of transparent rubbery amorphous or semicrystalline polymeric membranes. Most of the presently available soft lenses are based on poly(2-hydroxyethyl methacrylate) (PHEMA), its copolymers with poly(N-vinyl pyrrolidone) and other hydrophilic homopolymers and copolymers. These hydrogels are characterized by high oxygen permeability in contrast to polymers such as poly(methyl methacrylate) widely used for hard contact lenses. However, even in the case of soft lenses, the oxygen permeability may depend greatly on the water content of the polymer film, which in turn may be dependent on structural properties such as the crosslinking density and the degree of crystallinity.

OXYGEN PERMEATION

To analyze and evaluate oxygen transport through hydrogels serving as contact lenses, one has to model the general problem of gaseous diffusion through polymeric membranes. Considering a membrane as a homogeneous phase with one solute (oxygen) diffusing through it, one can write for isothermal systems (4):

$$N_{O_2} = cD_{O_2,m}\left[1 + \frac{\partial \ln \gamma_{O_2}}{\partial \ln x_{O_2}}\right]\frac{\partial x_{O_2}}{\partial z} + x_{O_2} N_{O_2} \tag{1}$$

Here N_{O_2} is the oxygen flux, $D_{O_2,m}$, is the diffusion coefficient of oxygen through the membrane, and x_{O_2} and γ_{O_2} are the mole fraction and activity coefficient of oxygen *in the membrane*.

For integration of this equation in terms of variables characteristic of the external phases, one needs to know the variation of the activity coefficient γ_{O_2} with mole fraction x_{O_2}. It can be assumed that these quantities are constant throughout the polymer film for most cases of soft lenses. Then this expression can be integrated between external phases, and across the polymer film thickness δ, using the partition coefficients $K^{w}_{O_2}$ of the oxygen with respect to an aqueous external phase, or Henry's law constant $K^{g}_{O_2}$ with respect to a gaseous external phase. Therefore, three cases of gaseous diffusion are analyzed, namely gas-to-gas (G/G) diffusion characterized by a permeability coefficient P_g, water-to-water (W/W) diffusion with corresponding permeability P_d, and gas-to-water (G/W) diffusion leading to a permeability P_{gd}. Integration of equation (1) under these assumptions can lead to expressions for the three permeability coefficients.

$$\text{W/W} \quad P_d = D_{O_2,m} K^{w}_{O_2}/\delta \tag{2}$$

$$\text{G/G} \quad P_g = D_{O_2,m} K^{g}_{O_2}/\delta \tag{3}$$

$$\text{G/W} \quad P_{gd} = P_d \left(\frac{K^g_{O_2}}{K^w_{O_2}} c^g_{O_2} - c^w_{O_2} \right) \Big/ \left(c^g_{O_2} - c^w_{O_2} \right) \tag{4}$$

The first two constants have been known in relevant literature as "dissolved oxygen" and "gaseous" permeability coefficients respectively (5-7). In contrast, the third permeability coefficient P_{gd} has been mentioned only once (8) and it is not extensively used. And yet, it is this permeability that is important in contact lens evaluation. With these definitions, equation (1) takes the convenient form:

$$N_{O_2} \left(1 - \bar{x}_{O_2} \right) = P \left(c^1_{O_2} - c^2_{O_2} \right) \tag{5}$$

where P is any type of permeability coefficient, $c^1_{O_2}$ and $c^2_{O_2}$ are the concentrations of oxygen in the two external phases, and $\bar{x}_{O_2}$ is the average mole fraction of oxygen *in the membrane*.

Here we analyze the dependence of P_g, P_d and P_{gd} on structural characteristics of hydrophilic crosslinked polymer films.

EXPERIMENTAL STUDIES AND DISCUSSION

A series of polymeric membranes (hydrogels) usually used in soft contact lenses were prepared. PHEMA hydrogels (Toyo Contact Lens Co., Nageya, Japan) were crosslinked with glyceryl methacrylate, cut in solvent-free state, and swollen in water at 34°C. Three types of poly(vinyl alcohol) (PVA) hydrogel membranes were also tested. Amorphous membranes (PVAA) were prepared by radiative crosslinking of a 10 wt% aqueous solution of PVA and finally swollen in water at 34°C. The number average molecular weight between crosslinks M_c was calculated (1) between 2,850 and 7,260 depending on the preparation conditions. Semicrystalline PVA hydrogels (PVAC) were produced by subsequent or by further annealing at 120°C for 30 minutes (PVAC2). In both cases the membranes were finally swollen at 34°C and their degree of crystallinity was determined as before (10). The degree of hydration H was determined as the ratio of weight of water in gel to weight of the hole gel at equilibrium with water at 34°C.

A permeation cell was constructed consisting of two half-cells connected by an opening of 12.7 mm diameter (9). The left half-cell was kept at constant temperature of 34°C and purged with oxygen, while the right half-cell was filled with distilled water. Gas-to-water experiments were performed, with oxygen being measured in the right half-cell with a Beckman 0260 oxygen analyzer.

The degree of hydration, molecular weight between crosslinks, thickness and gas-to-liquid dissolved oxygen permeability P_{gd} were measured or calculated for the various membranes tested.

First it is shown that for PHEMA hydrogels of the same average degree of hydration (samples S01-S05) of 25.10%, the permeability increased with increasing film thickness δ. A linear dependence is obtained by plotting P_{gd}^{-1} versus δ^{-1}. The intercept of this line (Figure 1) represents the value of P at infinite thickness, namely the "gaseous" permeability P_g (11). This value for PHEMA is $P_g = 1.205 \times 10^{-9}$ cm^3 (STP) · cm/sec · cm^2 · cm Hg, while the corresponding value for amorphous PVA is calculated as $P_g = 8.51 \times 10^{-9}$ cm^3 (STP) · cm/cm^2 · sec · cm Hg, again by extrapolition (samples S61-S65).

This marked difference in permeation behavior is due to the additional oxygen permeation resistance at the interface between water and hydrogel, when the measurement is made at C/W or W/W conditions (12).

At constant film thickness, the degree of crosslinking significantly affects the degree of hydration and the permeability. According to Yasuda and Lamaze (13) for solutes of size smaller than the pore size of the membrane, the permeability is an exponential function of [(1/H) – 1]. Figure 2 shows a linear dependence of oxygen permeability $ln\, P_{gd}$ on 1/H for a series of hydrogels of constant thickness (samples S41-S45). Extrapolating to H = 1.0 (pure water) one can determine a value of $P = 9.05 \times 10^{-9}$ cm^3 (STP) · cm/cm^2 · sec · cm Hg which is very close to the reported value of oxygen diffusion in pure water of 9.16 x 10^{-9} units.

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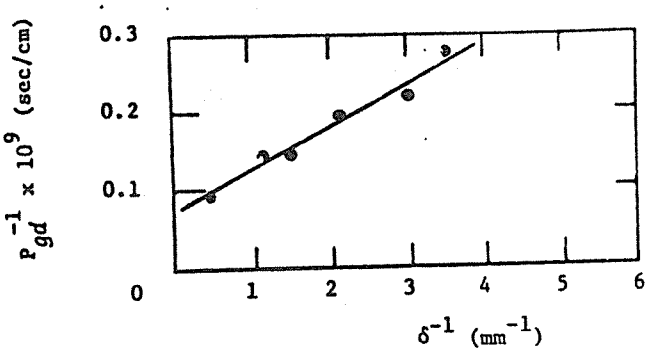

Fig. 1. Inverse oxygen permeability P_{gd}^{-1} plotted as a function of inverse thickness for PHEMA hydrogels with H = 25.10 at 34°C.

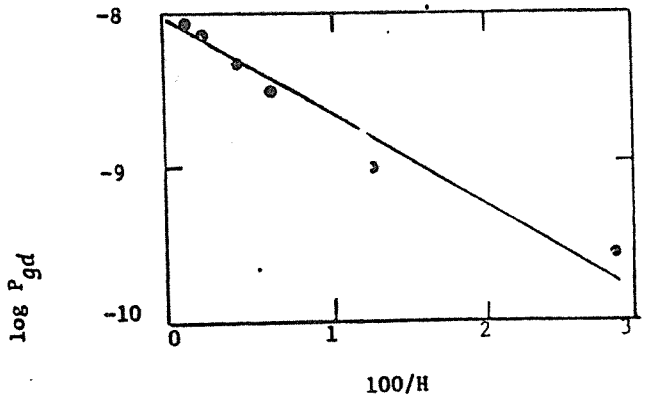

Fig. 2. Effect of hydration H on the oxygen permeability P_{gd} of amorphous crosslinked PVA hydrogels.

PROPERTIES AND APPLICATIONS OF OPHTHALMIC BIOMEDICAL POLYMERS

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Biomedical polymers are used to make therapeutic devices that are implanted in different body organs to correct or restore function. In ophthalmology, polymers are used for implants and contact lenses (CLs), which are placed on the surface of the eye.[1] Ophthalmic surgeons use polymeric devices to correct the optical function of the eye (ie, intraocular lens implants [IOLs] after cataract surgery)[2] and to restore vision (ie, vitreous implants and scleral buckling materials to repair retinal detachments).[3] Polymeric devices also are used to control abnormally high intraocular pressure in otherwise intractable glaucoma,[4] and experimentally in keratoprostheses,[5] artificial epithelium,[6] endothelial[7] and intracorneal implants.[8] Ideally, polymers used in ophthalmic surgery must be free of residual monomers. However, the cyanoacrylate adhesives, a kind of biomedical material, are applied to eye tissues in the monomeric state and polymerize in situ instantly to repair ocular perforations, ulcers, and possibly retinal detachments.[9]

Judging by the large number of CL users and the economic magnitude of the CL industry, an important use for synthetic polymers in ophthalmology is for the manufacture of these devices.[10] Of course, CLs are optical devices and must transmit visible light, but pigments and dyes are added to some cosmetic CL materials. There is also renewed interest in manufacturing CLs containing ultraviolet (UV) light-absorbing additives,[11] which can be dispersed or copolymerized in the CL material. Good oxygen permeability, water wettability, and resistance to fouling are the principal properties sought in CL materials, other than the obviously desirable optical and manufacturing properties and high chemical stability under normal use. Desirable properties vary with the manufacturing process. Thus, good lathing and polishing properties are required for lenses made on the lathe, but could be irrelevant for molded and cast lenses. Because

rubber is difficult to polish, producing good lens edges is a problem. There are many CL materials, and their physical properties determine their fitting characteristics on the eye; soft hydrogel CLs are supple and fit snugly onto the corneal surface, while rigid CLs fit loosely and move freely.[12] The latter must be made so that any flex on the lens provoked by the blink must recover instantly. CL materials also must be physically stable (a rigid CL must not distort upon hydration or dehydration) and be more resistant to dehydration under normal use than the currently available hydrogel lenses.[13]

The properties of the materials used for ophthalmic implants must be related to the ultimate use of the implant. IOLs must be transparent, but although most have a rigid optical portion of poly(methyl methacrylate), there is now interest in developing soft IOLs that can be inserted in the eye through smaller surgical incisions than the rigid lenses.[14] Filtration of UV rays by UV-absorbing moieties polymerized or dispersed in the IOLs also has become recently desirable.[15] Highly viscous but preferably viscoelastic solutions of biopolymers such as sodium hyaluronate (SH)[16] and/or chondroitin sulfate[17] or hydroxypropyl methylcellulose[18] are useful adjuncts in IOL implant surgery for maintaining anterior chamber depth during the introduction of the implant and for preserving the corneal endothelium.

Scleral buckling procedure materials, eg, silicone solid rubber, sponge, and acrylic hydrogels, for retinal detachment surgery must be soft and elastic, but transparency is irrelevant.[19] Vitreous implants are also desirable in certain difficult cases of retinal detachment surgery.[20] From a materials point of view, the main problem with intravitreous implants is the long-term tolerance of the substance used for the implants. Physiologic saline solutions, air, and gases, as well as SH solutions, are injected into the vitreous cavity with relative frequency during vitreoretinal surgery.[21] When a short-term vitreous substitute is required, these substances may perform well. However, for long-term vitreous replacement, the only substances used at this time are high-viscosity silicone oils (1000-10,000 centistokes) that are far from ideal.[22] The use of intravitreous silicone oil implants results in multiple complications, such as emulsification, glaucoma, intraocular membrane formation, cataracts, and corneal opacity.

Intraocular lipid solubility in silicone oil,[23] low interfacial tension with the intraocular fluids, and migration into the intraocular tissues are undesirable properties of the silicone oil for long-term vitreous implant. The ideal vitreous implant would be a cross-linked hyaluronic acid that could be injected into the eye without fragmentation.

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PREDICTION OF THE MOVEMENT CHARACTERISTICS OF SOFT CONTACT LENSES

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Soft contact lenses are worn by approximately 35 million people worldwide. New materials are being developed constantly with advances being made with increased oxygen permeability and improved surface resistance to deposition. These new materials display a range of mechanical properties[1] and some require novel lens designs to provide adequate on-eye performance.

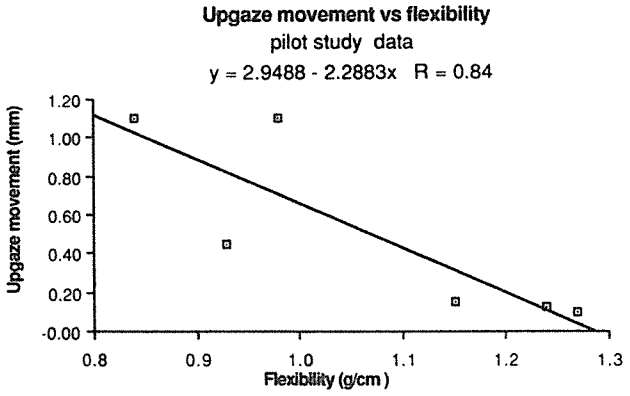
In this study we examined the relationship between the measured mechanical properties and fitting characteristics of soft contact lenses to provide a better understanding of those factors which are important in lens design[2]. Adequate lens movement is one of the indicators used to determine a successful fitting. It is important for the removal of metabolic waste products from the cornea[3], however, excessive movement can adversely affect visual acuity and comfort.

A series of soft lens materials with varying mechanical properties were obtained and were lathe cut into identical designs. Initially 3 materials, PHEMA 38%, Gelflex 60 and Gelflex 71 were selected for a pilot study. Two lenses of each material were cut and their movement characteristics were determined in a masked clinical trial. Upgaze and primary movement, centration and lag were determined and compared at 15 minutes and two hours after insertion. A video recording system on a modified slit lamp was used to record the on-eye behaviour and aid performance assessment.

Flexibility and Young's modulus were determined by inflating each lens with isotonic saline and measuring the pressures developed under the lens as a function of volume. The stress relaxation modulus was estimated maintaining a constant strain in a similar fashion and monitoring the pressure drop with time.

Variation of upgaze movement with lens flexibility results from the pilot study are shown in Figure 1. This reveals that as flexibility increases the amount the lens moves decreases.

FIGURE 1



In a full study we investigate five different materials and correlate their mechanical properties and on-eye performance. This information shows how laboratory measured mechanical properties can be incorporated in lens design so that on-eye performance can be predicted.

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BIO - ARTIFICIAL POLYMERIC MATERIALS

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Polymeric materials for biomedical applications should possess both chemico-physical and mechanical properties which are adequate to the end use, with opportune biocompatibility.

Many polymers already on the market show chemico-physical and mechanical properties comparable with those of the biological materials they must substitute, but they do not show sufficient compatibility.

On the other hand, biological polymers (fibrinogen, collagen etc.) show, of course, good biocompatibility but often inadequate mechanical properties and high production costs.

We had the idea to design new biomaterials based on blends or composites consisting of biopolymers and artificial (synthetic) polymers.

This lecture will describe the results obtained in the study of a new biomaterial produced by mixing synthetic polyurethanes (PU) with the plasma protein fibrinogen (FBNG) and subsequently transforming the fibrinogen into covalently cross-linked fibrin (FBN) by the enzymatic treatment with thrombin, factor XIIIa and calcium ions.

The fairly low fibrinogen release (15%) from the blend and the DSC analysis seem to prove the presence of strong interaction, operative on a molecular level between PU and FBNG. The transformation of the PU-FBNG bond into a PU-FBN blend is confirmed by DSC analysis, which shows the disappearance of a characteristic transition at 90 C present in FBNG and not in FBN.

This material has been successfully used for the production of small diameter vascular grafts and nerve guidance channels by spraying the blend of PU and FBNG over a rotating mandrel according to a phase inversion technique.

In vivo experiments carried out inserting the prosthesis (1.50 mm ID, 2.0 mm OD, and 1.5 mm long) in the rat infrarenal aortic position, showed significant resorption of the graft material with marked tissue invasion but poorer cell organisation and patency with respect to PU prosthesis.

However, an optimal balance between prosthesis degradation and tissue replacement will be found by varying the PU/FBNG ratio .

We are now studying other potential bio-artificial polymeric materials by bonding synthetic polymers with functional groups, with collagen and other bio-polymers. One or both of the components of the bonds are successfully cross-linked either by chemical or enzymatic treatments.

POLYMER MATRIX RARE-EARTH MAGNETS for MEDICAL APPLICATIONS

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BACKGROUND

Polymer-matrix magnets, often called polymer-bonded magnets, are as common as refrigerator doors. Their use in industrial applications is ubiquitous, yet there are few commercialized medical applications. The industrial polymer-bonded magnets are typically fabricated using high speed, low cost methods which produce sheets and strips of moderately efficient ferrite-bonded magnets. For such applications, magnetic field density and physiochemical stability are seldom criteria.

PURPOSE OF STUDY

This work was conducted to explore alternative manufacturing processes, polymer-matrix compositions and rare-earth material properties to determine if the concept of polymer-matrix rare-earth magnets could be adapted to biomedical applications.

MEDICAL APPLICATIONS FOR RARE-EARTH MAGNETS

Review of the clinical and patent literature reveals numerous inventions utilizing magnet materials for many functions. In most cases the commercial development of these devices has fallen short of initial expectation. In many applications the sintered magnets have been too limited in their design performance characteristics to be useful. Often the magnets are incompatible with encapsulating materials and have been known to corrode, cause tissue-compression necrosis or have such limited design range that they can not be utilized in the typical surgical population.

The flexibility of design available in polymer-bonded magnets led to the exploration of manufacturing processes and materials which could combine polymers typically found in medical applications with rare-earth magnetic powders to form uniquely suitable polymer-bonded rare-earth magnets. It was recognised that magnetic materials could be formed in the optimum shape for the medical applications, thus enhancing design properties to overcome reduced flux density (relates to attractive or repulsive force) inherent with polymer-bonded magnets.

SUMMARY OF RESULTS

Studies were conducted to evaluate injection moldable polyurethane and polyethylene and transfer-moldable silicone rubber elastomer. The available silicone rubber processing was limited and meant the magnet-samples could not be formed in the presence of a magnetic field. As a result, silicone samples for initial biostability studies were made, but

the majority of this study dealt with the injection moldable polyether-polyurethane matrix-magnets. Such samples could be formed in a specially constructed laboratory apparatus which allowed the composite material (pre-milled rare-earth powders and plastic pellets) to be injection molded into the disc-shaped cavity while being exposed to a strong electromagnetic field. The magnetic field caused the magnetic powders to orient according to the field while the polymer-matrix was still in the molten state. After cooling and removal from the mold, the formed discs were further saturated with electromagnetic field to develop full saturation properties. For the aging and biocompatibility studies, Pellethane polyether-polyurethane and Union Carbide medium density polyethylene were used as the polymer-matrix. Samarium-cobalt powders were acquired from Hitachi.

A simple aging study exposed samples to 100 F in Ringer's solution and in air for twelve weeks. Solutions (and control solutions without magnets) were periodically analysed for the presence of cobalt and samarium. Magnets were tested against control values for loss of flux density. Positive controls were sintered samarium-cobalt magnets. The solutions containing polymer-bonded magnets and the solutions stored as controls remained identical in inorganic content throughout the period of analysis; there was no detectable cobalt or samarium. In contrast, the sintered samarium-cobalt magnets leached cobalt into the solutions and stained the polypropylene containers.

Cell-culture studies were conducted using identically formed discs; some discs were polymer-controls and others were formed with magnetic powders. All samples passed cell culture cytotox testing. Soft tissue implant studies in albino rabbits were also conducted with these materials. Samples were extracted after eleven and twenty-two weeks post-implant. Gross histological examination of polymer-bonded magnetic materials and polymer controls were passively incorporated in a narrow band of fibrous encapsulation with no visible alterations to the healing pattern.

Samples of polymer-bonded rare-earth magnet discs formed with Pellethane were subjected to ESCA analysis to determine the nature of the surface. The surfaces were analysed for the presence of cobalt and samarium. It was determined that a polymer layer of at least 30 angstroms covered the entire magnetic disk.

From these studies it was concluded that the biocompatible properties were likely due to the thin layer of plastic formed during the molding process. Analysis of the polymer-bonding efficiencies and molecular weight distribution of the polymers after processing revealed that improved fabrication processes would be desirable in order to achieve maximum magnetic strength. Further research and development is warranted.

MODIFICATION OF POLYMERS FOR THE PREVENTION OF FOREIGN-BODY INFECTIONS

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Infection caused by catheters or polymeric implant materials has become a great problem in modern medicine (1). Although novel polymer materials with improved biocompatibility are in use and despite aseptic surgical procedure, foreign-body infections cannot be prevented totally. Bacteria from the skin or blood (during transient bacteremia) can adhere to and survive on almost all polymer materials, representing a permanent source for infections (2). Especially coagulase-negative staphylococci are able to survive on polymer surfaces, protecting themselves against host defense mechanisms and antibiotics by a barrier of extracellular substances ("slime") (3). Intravenous antibiotic therapy is therefore in most cases insufficient for the treatment of staphylococcal foreign-body infections, so that often the infected implanted polymer has to be removed (4).

Recently we described possible strategies for the prevention of foreign-body infections by modification of polymers, e. g. with radiation methods, and by incorporating antimicrobial substances in polymers to prevent bacterial adhesion or eliminate already adherent bacteria (5, 6). In the present study we report about our investigations on incorporation of various antibiotics into polyurethanes and a glow-discharge modification of polymers with the aim to create antiadhesive or antimicrobial polymeric surfaces.

Incorporation of antibiotics into polyurethanes was performed by a method described previously (6). The polyetherurethane was dissolved in an appropriate solvent and various amounts of antibiotics (0,75 to 4,5 weight %) added to the solution. For some antibiotics a cosolvent had to be used. After evaporation of the solvent, the antibiotic-containing films were dried in vacuo at 50° C. As antibiotics clindamycin (Upjohn, USA), flucloxacillin (Beecham, UK) and vancomycin (Lilly, USA) were used.

Drug release from the polymers was determined in a modified bioassay which is normally used for the determination of antibiotic serum levels. Small discs of the polymers (d = 6 mm) were incubated in 1 ml NaCl-solution for a certain length of time. 40 ul of this eluate were given into punched wells of an agar plate which was inoculated with a bacterial test

strain (clindamycin and vancomycin: *S. epidermidis* ST 2, flucloxacillin: *S. aureus* SG 511). After overnight incubation at 37° C the inhibition zone diameters were measured. With the aid of a standard curve antibiotic concentration vs. inhibition zone diameter the amount of released drug from the polymer discs could be calculated.

For the modification of the drug release kinetics antibiotic-loaded polymer films were irradiated in a ^{60}Co- γ-source with doses up to 5 Mrad (dose rate $1{,}8 \cdot 10^5$ rad-h^{-1}). Antibiotics irratiated with a dose of 5 Mrad showed the same activity as unirradiated antibiotics, as was demonstrated by measuring their minimal inhibitory concentration MIC) using *S. epidermidis* KH 11 as test strain. In a further experiment, clindamycin-containing polyurethane films were treated in a glow discharge reactor using various gases (helium, ethylene) (7). The discharge voltage was 3 KV at a pressure of 0,8 mbar, the discharge time 2 min. Drug release kinetics of these modified samples was determined as described above.

Bacterial adhesion experiments with antibiotic-loaded polyurethanes were performed in the following manner: *S. epidermidis* strain KH 11 was grown overnight on blood agar, washed three times in phosphate buffer solution (PBS) and resuspended in PBS to a final concentration of 3×10^7 colony forming units (CFU) per ml. In one experiment the bacteria were suspended in human pool serum instead of PBS. Small discs of the polyurethane films (d = 6 mm) were incubated in the bacterial suspension for 3 h at room temperature. After this, the polymer discs were transferred into 100 ml of nutrient medium (Müller-Hinton broth) and stored under gentle shaking at 37° C. After 24, 48 and 72 h the number of adherent viable bacteria was determined with an ultrasonification assay: Polymer discs were given into 10 ml PBS and stirred ultrasonically for 90 sec to remove the adherent bacteria. The number of adherent bacteria was then determined by a colony count method. Glow discharge treatment of polyurethane films with various plasma gases and monomers (acrylic acid) was performed in a parallel plate reactor by a method described earlier (8). Bacterial adhesion to uncoated and serum-coated glow discharge-modified polyurethanes was done in a bioluminescence assay by Ludwicka et al. (9).

Incorporation of the antibiotics flucloxacillin, clindamycin and vancomycin into the

polyetherurethane WALOPUR leads to devices from which the antibiotic is released after contact with an aqueous solution. The chosen antibiotics have a good antimicrobial activity against staphylococci which are the predominant organisms found in foreign-body infections. In the case of flucloxacillin-containing polymer films, a relatively constant drug release is observed up to 5 days and even more. For clindamycin, the main portion of incorporated antibiotic is released within the first 2 days, and after 4 days no measurable antibiotic concentration can be detected. With vancomycin-containing films, also a high initial release is observed lasting for ~5 days.

First experiments to modify the drug release characteristics of the antibiotic-loaded polymers by irradiation show that a dose of 5 Mrad leads to a more constant release of flucloxacillin over 5 days. Investigations of this phenomenon including infrared spectroscopy methods are in progress. Glow discharge treatment of both sides of a clindamycin-containing polyurethane film with helium as plalsma gas leads to a delayed release of the antibiotic in comparison with the untreated sample. Studies with other plasma gases (ethylene, propylene) are under investigation.

The experiments to measure bacterial adhesion on antibiotic-containing polymers were performed in a way that the polymer discs were first incubated in bacteria suspension in PBS to let bacteria adhere to the polymer surface (as it may happen during catheterization or surgery). After this the discs were transferred into a nutrient medium to enable proliferation of the adherent bacteria (as it may occur when the polymer is in contact with body fluids, e. g. blood). The initial adhesion of the bacteria to the polymer surface is not prevented by the antibiotic-containing polymer films, however, in case of clindamycin- and especially flucloxacillin-films, the number of adherent viable bacteria is drastically reduced. In case of flucloxacillin, after 24 h the number of adherent bacteria drops from 10^5 to less than 10^2, after 72 h less than 10^1 adherent cells are found. Vancomycin-containing films do not show this effect, which is probably due to the low amount of released drug being insufficient for a rapid killing of adherent bacteria. Bacterial adhesion ot glow discharge modified films is reduced if acrylic acid is used as monomer. Using plasma gases like N_2, O_2, NH_3 or others no reduction is observed, which is most probably due to an increase in surface roughness by the glow discharge treatment. After precoating with serum,

all polyurethane films show reduced bacterial adhesion.

The devices with clindamycin and flucloxacillin might be useful for the application as catheter materials for the prevention of early onset-infections which occur few days after catheterization or surgery. Recent studies have shown that conventional antibiotic therapy cannot be successful in such cases, as the extracellular slime substance prevents an elimination of the adherent bacteria (10, 11). Using incorporated antibiotics in catheters (or implant materials) seems to be more effective, and the doses required for bacterial elimination are lower than those administered during conventional antibiotic therapy.

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PLASMA SURFACE TREATMENT AND POLYMERIZATION FOR PRODUCTION OF BIOCOMPATIBLE SURFACES

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Abstract

Gas plasma (glow discharge) techniques have been used for surface modification of polymer materials for biomedical applications. In non-depositing plasma atmospheres, new chemical groups were introduced into the surface and varying degrees of hydrophilicity achieved. Fluorocarbon polymers were made water wettable, and improved attachment and growth of endothelial cells on the modified surfaces were obtained. In polymerizing plasmas, organic-polymeric thin films were deposited onto fluorocarbon and polyurethane substrates. A range of organic vapours were found useful for production of high quality polymeric thin films. Endothelial cell growth experiments indicated a marked improvement in cell growth for some of these films.

Introduction

The short range of interfacial forces causes only the chemical groups at the very surface of a polymeric biomedical device to interact with the environment. This surface chemical structure affects interactions such as protein adhesion and cell growth. The mechanical and the biomedical properties can be optimized independently by the surface modification of a bulk polymeric article.

Gas plasma techniques have attracted attention for surface modification because of their versatility, low penetration depth, and uniformity of treatment. Plasma techniques are applicable to all polymers but are most useful for the surface modification of fluoropolymers which are difficult to treat by conventional chemical methods. A number of workers have used gas plasmas to provide new surfaces on existing commodity polymers for the production of novel biopolymeric materials [1-6].

The two major classifications of plasma surface treatments are non-depositing and depositing. Non-depositing plasma gases chemically modify polymer surfaces to a depth of a few nm. On the other hand, polymerizing plasma atmospheres lead to the deposition of thin, cohesive plasma polymer films onto the substrate surface. In this case the effect is the creation of a thin film "skin" that governs environmental interactions of the composite. We

have explored both types of plasmas and obtained modified fluoropolymer and polyurethane surfaces with a range of contact angles to distilled water. The long term stability of the contact angles was found to be excellent in most cases, and plasma treated polymers showed uniform attachment and good growth of endothelial cells. Surface analytical spectroscopy techniques were used in an attempt to identify the chemical functionalities that confer wettability and improved support for cell growth.

Experimental

PTFE, FEP, Gore-Tex, and Pellethane polyurethane sheeting materials were used. Rectangular sheets of polymer substrates were attached to the faces of the electrodes in a custom built plasma reactor [7]. Typical parameters used were pressure 0.4 to 0.9 Torr and flow rate 6 to 15 sccm/min. Oxygen and argon were supplied from cylinders. Water vapour and the organic "monomer" vapours were obtained from the vacuum boiloff of the liquid held in a round bottomed flask. The water wettability was assessed using a modified commercial contact angle meter. Cell growth experiments were performed with bovine endothelial cells. After 48 hours the samples were stained and cell growth and morphology assessed by fluorescence microscopy.

Results and Discussion

1. Non-depositing plasma atmospheres.

Plasma treatments in atmospheres of air, oxygen, water vapour, and argon all produced increased hydrophilicity on Teflon, FEP and Gore-Tex sheets (Table 1) and the contact angles achieved were dependent on the power and the length of plasma treatment. Literature reports often describe plasma treatment times of many minutes; however, we have found that in our reactor 10 to 20 seconds are sufficient. Such short treatment times open up the feasibility of plasma treatment of substrates at transport speeds of commercial viability. In order to investigate the long term stability of the hydrophilic surfaces, some of the samples were kept in storage (at ambient temperature). The contact angles were found not to be measurably different for the air plasma treated samples after one year whereas argon plasma treated samples showed a slow increase in the contact angles. Previous work [8] on the increase in contact angles on polypropylene treated in an oxygen plasma was interpreted in terms of slow removal of the polar groups from the surface by thermally driven reorientation of polymer chains. The contrasting permanence of our oxidatively plasma treated surfaces of fluorinated polymers may partly be the result of a higher glass transition temperature of these polymers, and of crosslinking produced by the plasma treatment, a crosslinking that prevents

reorientation of the surface chemical constituents.

XPS analysis of air plasma treated PTFE showed a surprisingly low level of oxygen to be present. The C 1s peak contained, in addition to the still dominant CF2 signal, a broad peak at 284.8 eV assigned to mainly neutral carbon with a smaller C-O contribution. A significant level of C=O could not be ascertained underneath the high energy slope of this broad peak. It appears that following abstraction of fluorine in the plasma, some of the resulting radicals undergo oxidation, but more react by crosslinking. ATR-FTIR spectra showed only bands consistent with a fluorocarbon surface as the ATR sampling depth of ~ 2μm is excessive for detection of vibrations due to chemical groups produced by the plasma treatment to a depth of a few nm only. No evidence of changes in surface topography with plasma treatments was seen in SEM observations.

In endothelial cell growth experiments good growth with uniform morphological definition was obtained on the air plasma treated PTFE surface. Cell growth on untreated PTFE was much inferior; cells grew at a much slower rate and tended to stack onto each other in preference to attachment to new sites.

2. Depositing plasma atmospheres.

Plasma treatments using the organic monomers hexamethyldisiloxane, acrylonitrile and methyl methacrylate, as well as others, were able to provide coherent plasma polymer layers on the different substrates. The distilled water contact angles obtained depended on the monomer and the plasma conditions. Table 2 lists some selected results. Reassessment of samples after 13 months of storage showed no change in the contact angles. Spectroscopic analysis has been reported for some of the plasma polymer films [9], and for others analysis by XPS and ATR-FTIR is continuing.

Initial cell growth experiments with most of these samples of plasma treated fluoropolymers showed performance much superior to that on untreated polymers although with one sample some patchiness was observed, giving a uniformity of coverage of cells inferior to that obtained on tissue culture polystyrene. However, on many of the other plasma polymerized films cell growth was observed to be vigorous and even, resulting in a well spread and densely packed growth morphology. Cell growth experiments are continuing; but with the results obtained so far it has not been possible to elucidate a correlation between water contact angles, known surface chemistry, and the quality of cell growth.

While surface spectroscopic analysis has so far been unable to elucidate the chemical composition of the surfaces in sufficient detail to assign improved properties to the presence and density of specific chemical groups, it is clear that the improvements in cell growth are due to chemical modification of

the surfaces rather than changes in surface morphology. The increased support of cell growth must be due to the new chemical groups introduced by the plasma treatments, and perhaps also the cleaning off of surface contaminants.

Animal implantation studies are in progress in order to assess the biomedical compatibility and resistance to degradation of samples consisting of plasma polymer films on various substrates.

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Table 1. Contact angles, sessile (SCA), advancing (ACA) and receding (RCA), in degrees, of distilled water on untreated and plasma treated (for 30 sec) FEP samples.

Atmosphere	Power (W)	Pressure (Torr)	SCA	ACA	RCA
none	-	-	110	117	95
Air	12.3	0.60	78	92	21
Oxygen	12.3	0.63	86	91	25
Water	17.2	0.66	89	94	5
Argon	12.5	0.6	86	-	-

Table 2. Contact angles (in degrees) with distilled water of selected plasma polymer films.

Monomer	Substrate	SCA	ACA	RCA
Acrylonitrile	PTFE	84	90	20
	Gore-Tex	76	80	0
	"	95	101	0
MMA	"	77	91	20
HMDSO	"	100	114	80
	"	100	112	72
A-1	Pellethane	70	73	0
A-2	"	29	31	0
A-3	"	57	70	36

TEMPERATURE-SENSITIVE HYDROGELS FOR BIOMEDICAL APPLICATIONS

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INTRODUCTION

One phenomenon that has received significant attention in the past 5 years is that of expansion or collapse of hydrophilic networks near the theta temperature (1). The phenomenon seems to be of particular interest to controlled release technologists, since drugs incorporated into the hydrogel structure at one temperature can be released abruptly at another temperature due to collapse of the network structure (phase separation) (2). For example, Hoffman and his associates have reported the possibility of using polyacrylamides to release various drugs (3). It is also important in general biomedical applications where small temperature changes can lead to major swelling changes. In addition, Cussler and his associates (4) have utilized the same phenomenon as a method to separate proteins from electrolytic solutions.

THERMODYNAMIC ANALYSIS

The structural parameter defining the overall crosslinked structure of the network (5) is the number average molecular weight between crosslinks, $\bar{M}_c$, or the equivalent number average degree of polymerization between crosslinks, $\bar{N}_c$. The last parameter is defined by equation (1) where M_r is the molecular weight of the polymer repeating unit.

$$\bar{N}_c = \bar{M}_c / M_r \tag{1}$$

Methods of experimental determination of the value of $\bar{M}_c$ for highly swollen hydrogels (such as poly(vinyl alcohol)) or moderately swollen ones (such as PHEMA) have been reported. All these studies require that the network be placed in a thermodynamically-good or poor solvent and be allowed to expand to constant weight *isothermally*.

The actual size of a macromolecular chain between two consecutive junctions (crosslinks) of the network, r, when placed in a swelling agent is given by equation (2)

$$r = l\bar{N}_c^{\nu} \tag{2}$$

Here, l is the effective segment length, in our case the bond length between two consecutive atoms, and ν is a characteristic exponent for the system.

The thermodynamic dependence of ν is related to the temperature at which the swelling occurs. One is then reminded that in any polymer/solvent system (solution) as well as polymer network/swelling agent system (gel), there is a characteristic critical temperature for phase separation. When the molecular weight of the polymer is infinite, this temperature is known as the *theta* Θ *temperature*. In *good swelling agents* (with Flory interaction parameters, $\chi < 0.5$), the value of ν is 3/5 and the interactions between repeating units of the crosslinked chains are repulsive. Thus, swelling is achieved. The value $\nu = 3/5$ is reported by deGennes (6) and others, whereas $\nu = 0.588$ may be more exact (7). In *poor swelling agents* (with Flory interaction parameter $\chi > 0.5$), the value of $\nu = 1/3$ and attractive interactions between repeating units in the crosslinked chains prevail. At Θ conditions (with $\chi \sim 0.5$), the chains are thermodynamically ideal and $\nu = 1/2$, as the original Flory theories predict.

The problem under consideration is the variation of the swelling characteristics of a hydrogel as a function of

experimentation temperature, T. First, the experimental (or theoretical) value of the end-to-end distance between two consecutive junctions, $\bar{r}_{c,o}$, is recorded at the state of complete syneresis (collapse), i.e. in the unperturbed state (absence of solvent). Then, the expansion ratio, α, is defined as

$$\alpha = \bar{r}_c / \bar{r}_{c,o} \tag{3}$$

where $\bar{r}_c$ is the corresponding value at any other condition. A large value of α indicates *swelling*, a low value indicates *syneresis*. The variation of the temperature is usually expressed in terms of the dimensionless temperature deviation, τ, defined as

$$\tau = (T-\Theta)/\Theta \tag{4}$$

where Θ is the critical temperature used as reference. The transitional characteristics of the macromolecular chains are expressed in terms of the change of temperature using the parameter z which is defined as

$$z = \frac{\beta(1+\frac{1}{\tau})^2}{\bar{N}_c} \tag{5}$$

Then, the expansion coefficient, α, is easily calculated from the following relationship.

$$\alpha^2 = z^2(3-2z) + 6z^{1-2v}\left[\frac{1-z^{2v+1}}{2v+1} - \frac{1-z^{2(v+1)}}{2(v+1)}\right] \tag{6}$$

Since the equilibrium volume degree of swelling of a hydrogel, Q, is related to α as expressed by equation (7)

$$Q = \alpha^3 \tag{7}$$

it is possible to fully describe the effect of temperature by combination of equations (4) through (7).

EXPERIMENTAL PART

Copolymers of various hydrophilic systems were prepared by bulk copolymerization of N-isopropyl acrylamide (NIPA) with vinyl acetate (VAc), N-vinyl-2-pyrrolidone (NVP), methacrylic acid (MAA) or 2-hydroxyethyl methacrylate (HEMA) in the presence of AIBN as an initiator.

The resulting cylinders were cut to form discs which were swollen in buffered solutions. The equilibrium degree of swelling was measured.

DISCUSSION

For most hydrogels, the Θ temperature is an upper critical miscibility temperature (UCMT). Above Θ, the polymer network is in a thermodynamically good solvent ($\chi < 0.5$) and $v = 0.588$. Thus, equation (7) becomes

$$Q = [-0.12z^3 + 0.24z^2 + 0.88z^{-0.176}]^{3/2} \tag{8}$$

Below Θ, $\nu = 1/3$ and equation (8) becomes

$$Q = [0.25z^3 - 0.6z^2 + 1.35z^{1/3}]^{3/2} \quad (9)$$

Figure 1 shows the dependence of the equilibrium volume degree of swelling on the normalized temperature deviation, τ, above the Θ temperature using equation (8). It can be shown that major gel collapse occurs as the temperature approached Θ.

Experimental results of the equilibrium degree of swelling of various crosslinked hydrogels containing N-isopropyl acrylamide are shown in Figure 2 as a function of temperature. The overall syneresis (collapse) behavior can be readily predicted by the previously developed theory.

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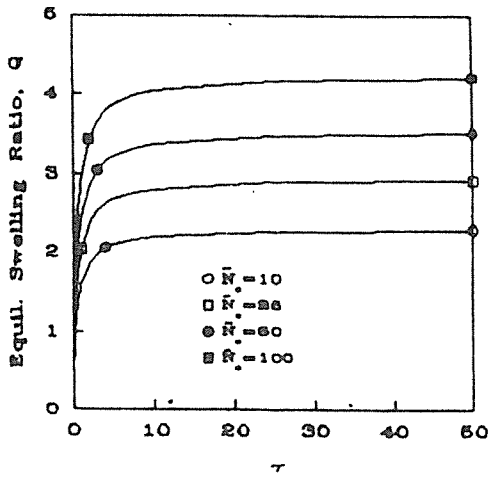

Fig. 1. Equilibrium swelling as a function of normalized temperature above Θ for various $\bar{N}_c$ values.

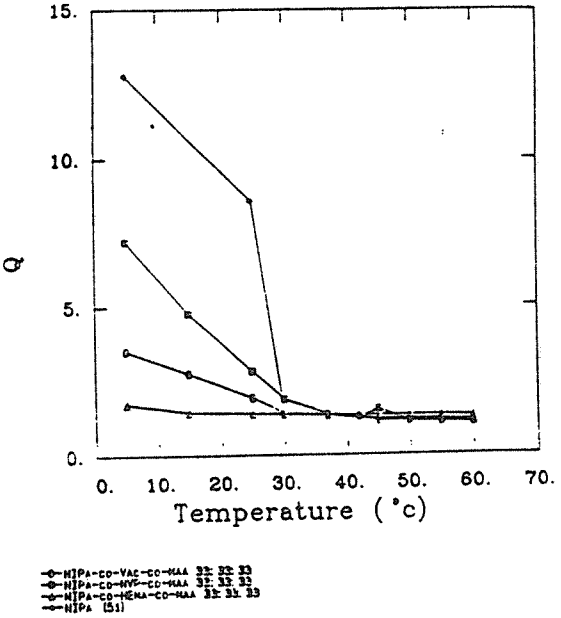

Fig. 2. Equilibrium swelling of various N-isopropyl acrylamide-containing gels as a function of temperature.

AN IN VITRO MODEL OF QUANTITATIVE CYTOCOMPATIBILITY ASSESSMENT RELEVANT TO DIFFERENT CLASSES OF BIOMATERIALS

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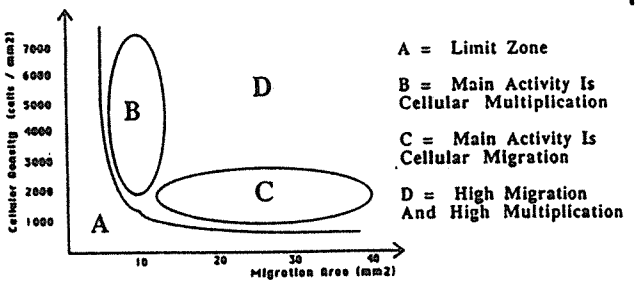
Abstract :

The cytocompatibility assessment of biomaterials has been defined by measuring "in vitro" three biological parameters involved at the interface tissue-material (cell growth, migration and attachment). Computerization of the data makes the model reproducible and easy to apply. For each class of biomaterial (cardio-vascular, orthopaedic, dental and ophtalmological) we used the tissues belonging to the future implantation site, that are respectively endothelium, cartilage, gingival and cornea, with reference to positive (toxic) and negative (non toxic) control materials. The tissue is cultivated in direct contact with the biomaterial and in contact with its extract. We obtained different responses depending on the tissue and/or the biomaterial used, that demonstrates the sensitivity of the model. Both extracts and direct contact studies allow to define respectively the cytotoxicity of the biomaterials and to preselect it as a function of their biological requirements.

At present, the "in vitro" methods proposed by standard associations to assess the cytocompatibility of a biomaterial are using culture techniques and cell lines that do not take in account the tissue/material surface relations and limit them to a semi-quantitative measurement of this cytotoxicity (1). The organotypic culture technique seems a more convenient method as it allows to cultivate tissue fragments, even whole organs, at the interface air/medium. These culture conditions preserve the interactions between the different cellular constituants necessary for the tissue functions and allow tissues or organs to grow and/or survive in metabolic conditions closed to those observed "in vivo".

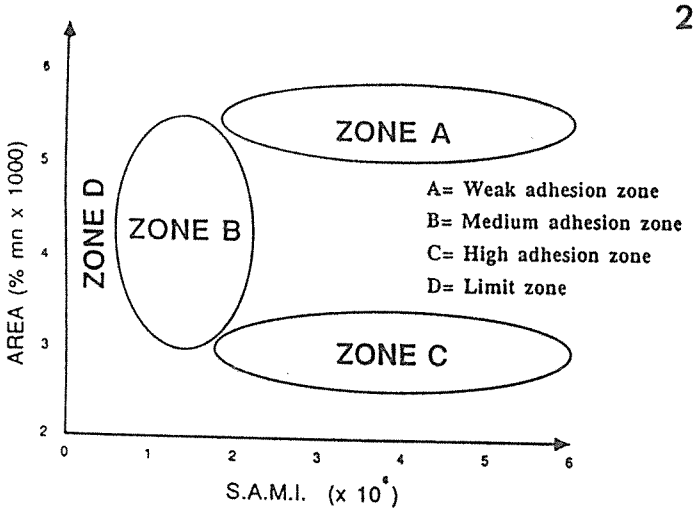
We have perfected an "in vitro" model that allows to measure quantitatively three biological properties (cell growth, migration and adhesion) involved at the interface tissue/material relevant to the different classes of biomaterials. For each class of biomaterials, cardio-vascular, orthopaedic, dental and ophtalmological, we used respectively, vascular endothelium, cartilage, gum and cornea. Studies have been performed both by direct contact and by adding the leakage product of each material$_2$ (5 days at 37°C in nutrient medium - 5 cm^2/ml). In that case, the tissue explants are cultivated in contact with the plastic for cell culture. The following materials, proteinic polyester, polymeric artificial ligament, dental resin and polymeric contact lenses have been tested with reference to positive toxic (PVC) and to negative non toxic (plastic for cell culture : Thermanox^{tm} Lux) controls. The tissue samples collected from animals (chick embryos and new born rats) were explanted on an agar nutrient medium as described before (2). A computerized analysis allowed to provide, area of cell migration, cellular density, percentage of cells released as a function of time (enzymatic dissociation) and the adhesion cell modulated index or SAMI (3,4). These data are reported on two diagrams by plotting the cellular density as a function of migration area (Diag. 1)

1



and the adhesion behaviour as a function of SAMI (Diag. 2). Tissue fragments cultivated on a phenol solution containing medium allowed to define a gradient of toxicity in the limit zone (Diag. 3).

2



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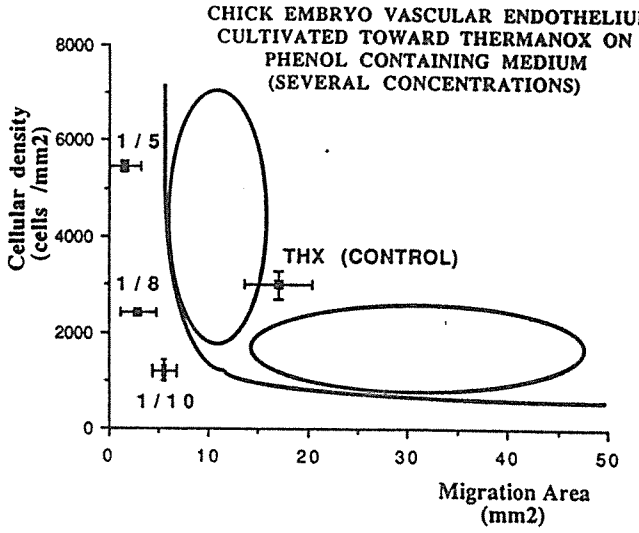

Our results pointed out different responses depending upon the tissues and the biomaterials used and showed that experiments performed with the extracts precise the cytotoxicity of the materials as those performed by direct contact outline quantitatively the biofunctional involvements of the tested materials.
This easy, sensitive and reproducible technique that shows a good correlation with the "in vivo" experiments, allows to classify and thereafter to choose materials as a function of their biological requirements.

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COMPLEX-FORMING HYDROGELS SENSITIVE TO PHYSIOLOGICAL CONDITIONS

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INTRODUCTION

Polymer networks which exhibit changes in swelling or permeability with a specific stimulus such as a change in temperature or pH of the surroundings have recently been considered for applications ranging from controlled drug release to separations (1,2). One way of regulating swelling, permeability and mechanical strength of polymer gels is to control the formation of complexes between complementary chains in the gels (3). Polymer complexes may exhibit physical properties which are very different from those of the parent polymers. Osada (3) used this approach to regulate the degree of swelling and permeability of poly(methacrylic acid) membranes by exposing the membranes to poly(ethylene glycol) solutions. The complexes of these two polymers resulted in shrinkage of the poly(methacrylic acid) membranes and dramatic changes in membrane permeability.

Here, we report the properties of copolymer networks which contain poly(methacrylic acid) chains to which poly(ethylene glycol) chains are grafted. These materials contain both complexing constituents in one network. The addition of a second component to induce complexation is not necessary. Furthermore, the property changes accompanying complexation are expected to be reversible, due to the covalent binding of the complexing polymers to one another.

EXPERIMENTAL

Hydrogels based on graft copolymers of poly(ethylene glycol) on poly(methacrylic acid) were synthesized by a free-radical copolymerization and crosslinking reaction. The monomer poly(ethylene glycol) methacrylate was synthesized by the acylation of poly(ethylene glycol) or methoxy poly(ethylene glycol) with methacryloyl chloride. The resulting poly(ethylene glycol) methacrylate was reacted with methacrylic acid and tetraethylene glycol dimethacrylate to form networks of poly(methacrylic acid-g-ethylene glycol). Swelling of networks with various pendant chain molecular weights and compositions was studied in water as a function of pH, temperature, and ionic strength. The swelling was also examined as a function of solvent composition using various alcohols as cosolvents with water.

The stress versus extension of polymer strips in the swollen state was studied for different network compositions with aqueous as well as alcoholic solvents. Finally, the permeability of copolymer membranes was examined as a function of solution pH and temperature.

RESULTS AND DISCUSSION

The copolymer networks exhibited large changes in swelling and solute permeability with changes in pH, temperature and solvent composition. Degrees of swelling were large at basic pH conditions, typically exceeding 95 % water, and as low as 25 % water in acidic conditions. In acidic media, the poly(methacrylic acid) constituent was protonated and formed hydrogen-bonded complexes with the poly(ethylene glycol) chains (4), giving rise to a relatively hydrophobic structure with a low degree of swelling and low permeability to hydrophilic solutes. Upon neutralization of the poly(methacrylic acid), the complexes were decomposed and the resulting polyelectrolyte gel exhibited large degrees of swelling and solute permeability. Complex formation was seen with poly(ethylene glycol) molecular weights as low as 200 in graft copolymer networks, but not in systems where the poly(ethylene glycol) was simply dispersed in the poly(methacrylic acid) network. This result indicates that complex stability in graft copolymer is greater than in polymer mixtures. Furthermore, swelling minima were seen in systems containing equimolar amounts of methacrylic acid and ethylene oxide functional groups, indicating that the complex stoichiometry is 1:1.

The swelling and solute permeability in aqueous media were found to depend on temperature. Largest degrees of swelling and permeability were found at low temperatures, with reduction in these properties with increase in temperature. These results indicate that complex formation is promoted by increasing temperatures and are consistent with the idea of hydrophobic stabilization of poly(methacrylic acid) complexes (5). The response of swelling to temperature was found to depend on molecular weight of the pendant chain, with largest changes occuring with the lowest molecular weight chain. Thus, complexes involving low molecular weight pendant chains are less stable than those involving high molecular weight chains. These observations are consistent with the idea of cooperativity in stabilization of macromolecular complexes (4,5).

Mechanical properties were found to depend on monomer ratios, polymer pendant chain lengths and swelling agent. In general, polymers containing large amounts of methacrylic acid were found to posess a higher elastic modulus than those rich in poly(ethylene glycol) methacrylate for identically prepared samples. This may be attributed to the increased tendency of poly(ethylene glycol) methacrylate polymers to undergo cyclization during the polymerization as a result of the lower concentration of reactive vinyl groups (6) present in systems with large inert pendant chains. Polymer networks in the complexed state were found to have higher elastic modulus than those in the uncomplexed state. This effect was largest for networks with large pendant chain molecular weight.

CONCLUSIONS

Networks of poly(methacrylic acid-g-ethylene glycol) were studied with regard to swelling, solute permeability and mechanical properties. All three of these properties were found to be highly dependent on the pH, temperature and composition of the swelling agent. This dependence was attributed to the reversible formation of polymer complexes between the poly(methacrylic acid) and poly(ethylene glycol) portions of the network.

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THE FAILURE ANALYSIS AND MATERIAL PROPERTIES OF SUTURES

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ABSTRACT An essential requirement of sutures is for them to exhibit adequate strength for their intended application. It is also important for any group of sutures to demonstrate a low variability in their material characteristics since then the surgeon will have confidence that the material has a high reliability.

Two brands of a polypropylene suture and a copolymer suture were subjected to tensile tests. The polypropylene sutures failed at an average load of 425g whereas the copolymer failed at 513g. The variance of the failure loads for the polypropylene materials was much higher than that of the copolymer materials and this may be attributed to pre-existing defects and flaws within the materials.

1. INTRODUCTION

A suture material can be broadly defined as a thread which is used either to close wounds or for ligature applications. There is no suture which is suitable for every application since each individual requirement may vary. Thus sutures may be classified under headings such as organic or synthetic, and absorbable or non-absorbable (1). The suture must meet a number of requirements. For example the "handling characteristics" (2) include properties such as the tissue drag, the ability to run and hold a knot, and the suture flexability. A final requirement is for the material to exhibit adequate strength so that it can withstand any processing or handling forces (3) as well as perform the intended function of a suture. It is also important for the above material characteristics to be well defined and reproducible since then the surgeon can have confidence

that the suture will be reliable under conditions of critical usage (4).

The present work focuses on the suture material properties of failure force, extension, and compliance; and examines their reliability by measuring the variance of these properties for a statistically significant number of tests.

2. MATERIALS AND EXPERIMENTS

Two synthetic non-absorbable materials of gauge 6/0 (0.070 to 0.099 mm in diameter) were selected for this study. The sutures were of polypropylene and a copolymer which can be described as a 'butester'. The polypropylene sutures were obtained from two different manufacturers.

The sutures were tensile tested in an Instron servo-hydraulic machine. The gauge length was 50 mm and the suture was attached to each crosshead by wrapping it at least three times around a 6 mm diameter pin. Up to three tests were obtained from each 75 cm long suture and at least 36 tests were performed on each suture with the stroke rate set at 5 cm min^{-1}.

Scanning electron microscopy was carried out on the as-received and some of the fractured specimens. These studies were aimed at characterizing any surface features of the sutures and relating these to the observed material properties. The suture materials were gold coated prior to the microscopy. The SEM was operated at less than 10kV to prevent damage to the materials under examination.

3. RESULTS

Table 1 summarizes the material properties of the sutures, where A and B refer to the polypropylene materials and C to the butester.

The large variance of the two polypropylene materials (sutures A and B in Table 1), in combination with similar mean values, indicates that their material properties can not be readily distinguished from each other. However the butester material has a significantly lower variance as well as a greater failure force, a

Table 1. Material Properties of Sutures

Property	Suture Type	Mean	Standard Deviation	Variance (%)
Failure load (g)	A	407	41	10
	B	448	48	11
	C	513	14	3
Extension to failure (%)	A	66	12	18
	B	48	16	34
	C	73	3	5
Compliance (mm N^{-1})	A	6.0	0.4	8
	B	4.9	0.4	9
	C	8.3	0.2	3

greater extension at failure, and a higher compliance.

4. DISCUSSION

It is believed that the variability in material properties may be related to the intrinsic nature of the materials. For example the as-received polypropylene materials exhibited surface flaws which were oriented along the longitudinal axis of the suture. These features open up upon the application of load and lead to a fibrillation mode of failure where the overall cross section of the suture is not evenly stressed. Thus the most highly stressed portion of the suture initially fails; which, in turn, raises the stress concentration for the remaining portion of the suture. It should be pointed out that the surgeon usually, unknowingly, recognises this failure mode as a "loose thread" or "free-end" in the wound that is being closed.

The butester suture on the other hand exhibited a relatively smooth and defect-free surface and did not fibrillate on fracture. The fracture surface of this material was oriented perpendicular to the suture diameter. The overall view is that the butester was more reliable (i.e., a lower variance in materials properties) than the polypropylene materials because their manufacturing schedule lead to an intrinsically more homogeneous material with a surface which was comparatively free of defects.

It should be remembered that an improved reliability may not necessarily

infer that one material should be preferred over another. Thus the absolute magnitude of the parameter is of importance; and for example, most applications of sutures would call for a material property which exhibited the greatest failure force. Also a highly compliant suture will maintain the opposing edges of a wound in close proximity and thus a high extension prior to failure is desirable. However it should be cautioned that these desirable properties need not necessarily correlate to the optimum handling characteristics of the suture.

5. CONCLUSIONS

1. There was no significant difference between the material properties of the two polypropylene suture materials.

2. The copolymer suture exhibited a lower variance in mechanical properties than the polypropylene materials.

3. The high variability in material properties of the polypropylene sutures arises from the influence of surface flaws and this is reflected by a fibrillation mode of failure.

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SYNTHETIC vs NATURAL MEMBRANES

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Living systems are built around membranes, of which there must be many hundreds of different types in any body. As well as containing molecules, organelles, organs and the whole body, they regulate both in kind and in quantity what goes in and out of the system which they surround. Thus they have a prime role in regulating metabolism by processes of reverse osmosis, ultrafiltration, ion selection and molecular fractionation.

Independently the chemist has created membranes of simpler, but totally different, chemical composition which duplicate some of the functions of natural membranes. Though crude by comparison with nature, the synthetic membranes can now be used to sustain life in many conditions which were formerly lethal.

In practice only membranes from the eyes, skin, lung and kidneys can be replaced, usually with imperfect function, and for various but limited times.

Loss of 50% of the skin was formerly fatal. Now a number of companies are marketing artificial skins, some of which are reputed to replace 90% of the original. These usually have a collagen layer(s) to simulate the dermis, and a silicone rubber outer surface to simulate the epidermis. This provides mechanical protection until reconstitution occurs with absorption and replacement of the collagen. One approach seeds the collagen layer with fibroblasts cultured from biopsy samples to give a "living skin equivalent". This has many of the functions of skin, and minimizes scarring, but it takes time to prepare due to the culturing step.

The cornea is essentially a transparent layer of collagen subject to damage and opacity due to disease. Transplants of functional corneas from cadavers is now widely practiced but the

supply is insufficient to meet the demand. Techniques are being developed to use collagen from other sources as a direct replacement. Synthetic polymers such as polysulphone and hydroxyethylmethacrylate hydrogels can be shaped and inserted within the cornea to correct errors in diffraction. The procedures are still experimental, and at least with polysulphone are fraught with hazard as the material is impervious to the nutrients necessary for corneal health.

Lung function is essentially a gas exchange across a membrane. The whole lung function is must be taken over for some hours during each of the 600,000 coronary bypass operations performed each year. This is done with a throw-away hollow fibre exchange unit with hydrophobic fibres of, for example, polypropylene. The few hours necessary for the operation is approaching the limit of this technology, which is unlikely to be used outside the operating room or its environs.

The applicatio of synthetic membranes which is most successful in the long term must be in hermodialysis to replace kidney function. Some sufferers of end-stage renal disease now have survived in reasonable health for 25 years by 2-3 time per week dialysing their blood through hollow fibres against a hypertonic solution of salts. The fibres may be hydrophylic (cellulose, cellulose diacetate, diethylaminoethyl cellulose or polyetherpolycarbonate), or hydrophobic (polysulphone, polyacrylonitrile, polyamide, cellulose nitrate or polymethylmethacrylate). Recently hybrid copolymers have been produced, though regenerated cellulose remains the most popular. All fibres pass urea and creatinine, the major toxins in urine, satisfactorily, they differ mainly in their ultrafiltration capacity which must be controlled at the machine. There are minor differences for fine tuning in respect to immunogenicity, trace impurities, and the handling of molecules larger than urea and creatinine.

Since 1975 the patients own peritoneal membrane has been widely accepted for dialysis. By introducing the dialysing solution directly into the peritoneal cavity through a silicone rubber tube through the

abdominal wall, plasma components are removed from the capillaries into a hypertonic solution of glucose and salts. The process has been refined to such an extent that 30% of 2,500 dialysis patients in Australia prefer it to other methods. Its advantage is that it is a continuous process which does not require attachment to a machine and allows the maintenance of a relatively normal life style. It is better than hemodialysis at removing some of the molecules larger than urea and creatinine, and it can preserve residual renal function better. The peritoneum stands up well to its new role, but greater vigilance is needed to minimise infections of the peritoneum and the catheter exit site.

The search is continuing for membranes with enhanced long term biocompatibility and functionality. These could be used not only to improve the traditional applications but also to open new oportunities, as in the encapsulation of pancreas islet cells in the treatment of diabetes, and membranes in biosensors.

PREPARATION OF BIOMEDICAL INTERFACE MATERIALS USING RADIOFREQUENCY PLASMA POLYMERIZATION

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Introduction

The surface or interface, of a biomaterial is one of the most important factors that determines biocompatibility. However, the optimum bulk properties of existing biomaterials are rarely coincident with optimum surface properties. Consequently, any improvement is dependent upon the ability to optimize the material's surface without adversely affecting its bulk properties. Surface modification using radiofrequency (RF) plasma synthesis methods is a surface specific approach, inherently suitable for achieving these goals, with a wide range of biomaterials. Our recent studies have been directed toward realizing the outstanding potential of this technique for preparing polymer films with potential use as biomedical interface materials.

Methods

N-vinyl-2-pyrrolidone (NVP), n-hexane and hexamethyldisiazane (HMDS) were used as monomers in the plasma polymerizations. The reaction system[1] consisted of a tubular reaction chamber inductively coupled to an RF power supply (13.56Mz, with matching unit), a vacuum system and a gas inlet system. The thickness of polymer films, deposited on silicon wafer pieces, was determined from ellipsometery measurements. Water contact angles for films deposited on glass slides were measured by the sessile-drop method. The adhesion behavior of films deposited on glass and aluminium was observed qualitatively by boiling and sonication in water. Cyclic voltammetry measurements in a 10mM solution of hexacyanoferrate(III) in deaerated buffer, were obtained for films deposited on gold electrodes. A Surface Science Model SSX-100 ESCA spectrometer was used to obtain surface compositions and high resolution C_{1s} spectra of films deposited on silicon. A Digilab FTS-60, FT-IR spectrometer with a ATR unit; was used to obtain IR spectra of films deposited directly onto the germanium IRE.

Results and Discussion

Hydrophobic films (0.04-0.5 μm thick) with good adhesion properties and typical water contact angles of greater than 85 deg., have been prepared from HMDS (PPHMDS) and from hexane (PPHEX). PPHMDS is a hard, highly crosslinked polymer, while PPHEX provides a softer film, probably reflecting a lower crosslink density. Sensitive cyclic voltammetry measurements performed on a 400A PPHEX film indicated that the thin film completely covered (insulated) the electrode with no apparent defects. Polymer films (0.1-1.0 μm thick) derived from NVP have been prepared[1] with advancing water contact angles for films on glass which ranged from 24-41 deg., depending on the plasma energy reaction conditions. Receding contact angles usually approached zero, after the first receding angle measured, indicative of the hydrophilic nature of the films. This behavior was supported by swelling ratio measurements which showed that PPNVP films absorb water up to 52% by weight. The hydrophilic film can be covalently bonded to a polymer substrate, but in aqueous media it has poor adhesion to non-organic materials. To circumvent this, we have developed a successful layered film procedure for preparing adherent hydrophilic films. A thin film (<0.1 μm thick) polymerized from hexane provides an adherent protective coating for the substrate material and covalent bonding sites for the outer hydrophilic layer polymerized from NVP. The two monomers were copolymerized for a short period during the transition between monomers, to provide a covalently bonded diffuse interphase.

Our preliminary studies, using plasma polymerization methods, have shown that reproducible hydrophobic and hydrophilic films can be prepared. Variations in polymer composition can be accomplished by the appropriate choice of monomer and reaction conditions. Adjustments to the experimental procedures enables the surface modification of a wide range of potential substrate materials.

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"CRITERIA FOR EVALUATING NEW SYNTHETIC BIOMATERIALS FOR USE IN VASCULAR GRAFTS"

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The Omniflow vascular graft is a composite of ovine collagen (mainly types I and III) and polyester mesh. The blood contact surface of the prosthesis consists of haemocompatible tissue.

The long saphenous vein continues to be the conduit of choice for arterial substitution; however when it is unavailable, unsuitable or insufficient, an alternative is required. Omniflow, being a bio-synthetic composite, combines the advantages of a synthetic (readily available, variety of dimensions etc.) with those of a biological prosthesis (superior haemocompatible flow surface and resistance to infection).

It is the purpose of this paper to detail the essential performance criteria that a vascular graft needs in order to be a successful prosthesis and to illustrate how these criteria can be applied to select new biomaterials for prosthesis design.

In their review paper, Pourdeyhimi and Wagner[1] suggested that future research in the vascular prosthesis area should be directed particularly towards optimization of graft compliance; also the need for proper testing procedures to evaluate the properties and performance of the artery/graft system was highlighted. Hence, our approach has been to focus on key performance and structural criteria as much as possible. As such, we evaluate:

a) Haemocomatibility and Histological Response, [8]

b) In-Vitro Tests [2,3,4]

c) In-Vivo Studies (using the Dog as a model), [5,8,9], &

d) Clinical Studies. [6,7]

Haemocompatibility is seen as perhaps the most critical of graft parameters, and is defined as "...the inability of an artificial surface to activate the intrinsic blood coagulation system

or to attract or alter platelets or leococytes".[8] Hence thromboresistance is assessed by measuring the affinity of the flow surface for blood platelets; a twin artificial circulation unit is used in this procedure. The lower the platelet consumption, the more haemocompatible is the surface. This test is complimented by a thrombus-free surface method, a low-flow procedure which determines the extent of blood clotting and clot adherence to the surface.

Given the bio-synthetic nature of the prosthesis, detailed histological techniques are used to study the graft microstructure and to evaluate the reaction of the graft to contact with blood and body tissues.

In-Vitro testing confirms the graft's surface characteristics and durability. Internal reflection spectroscopy determines the unique "fingerprint" of the blood surface, which resembles that of the natural artery in many respects.[8] Critical surface tension is in the range 20-30 dynes/cm^2, comparable to the saphenous vein.[2,8]

Compliance, a measure of the radial elasticity of the graft, is reported to be important to graft performance.[1] Abbott and Cambria[8] showed that better in-situ functionality corresponds directly to greater (relative) compliance. While not yet equivalent to the natural artery, the graft's performance is deemed adequate, but clearly needs to be improved.

The grafts have been found to be stable after they have been subjected to pressures up to 150kPa. This is well in excess of the physiological blood pressure (20kPa), and indicates that the graft integrity will be maintained over long periods.

Shrink temperature, or the temperature at which the tissue contracts, is a measure of intramolecular cross-linking which imparts additional strength to the tissue. Temperatures in the range 79-83^{o}C are obtained typically, indicating a high degree of cross-linking. These durability tests are confirmed by additional evaluations which include suture-hold strength and accelerated fatigue testing.[8]

In-Vivo studies are based on a model with the following characteristics, i.e.:

a) Young adult greyhounds - Common Iliac/Aortic/Bilateral Femoral interposition,
b) Length 8cm,
c) Anastomoses 1cm, &
d) No antiplatelet therapy.

Although this model may not be the most challenging in which to verify the degree of haemocompatibility, it has been found to be extremely useful in providing stressful haemodynamic conditions to challenge the durability of the graft. With different series extending over some seven years, graft patency exceeds 70% in all cases.[8]

The prosthesis has also been evaluated clinically in Australia and Europe since 1983, and is currenlty undergoing similar studies in the U.S. It has been used for peripheral revascularization when the saphenous vein has not been suitable or reserved for future use. The 18 month patency rate using the cumulative lifetable method of 132 implants is 77%.[8]

The above combination of procedures has evolved into a protocol which has produced a successful clinical vascular prosthesis; details of successful relevant studies clearly illustrate the same. Hence, many of Omniflow's performance criteria approach those of the human saphenous vein, although further parameter optimization is still needed to produce the "perfect" graft.

This presentation discusses the application of our experience in developing the Omniflow prosthesis in the evaluation of synthetic prosthesis fabrication from novel biomaterials.

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THE RELATIVE CONTRIBUTION OF FIBRONECTIN AND VITRONECTIN TO ENDOTHELIAL CELL ADHESION ON CHEMICALLY DEFINED SUBSTRATES

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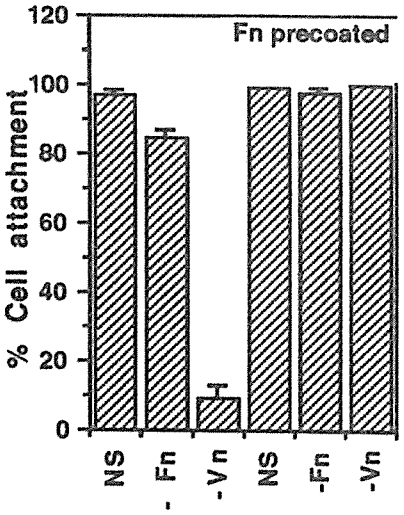
One approach to the design of vascular prostheses has been the selection of materials which by their chemical nature preclude thromboembolism. Two approaches are currently pursued: the first aims to select materials which are biologically non-interactive and by the chemical nature of the surface preclude thrombus formation. The alternative approach, which we have pursued, is to provide a substrate which is suitable for the support of endothelial cells, which themselves would provide a non-thrombogenic surface. We have investigated the potential value of sulphonated surfaces for endothelial cell attachment and growth, mindful of the likely antithrombogenic nature of such a chemical surface, and particularly in view of the fact that surfaces presenting negatively charged groups (eg carboxyl groups) have been held to provide a suitable substrate for cell attachment and growth. One polymer which provides pendant sulphonic groups is the perfluorosulphonate ionomer Nafion (Du Pont). Nafion has been shown to support bovine endothelial cell attachment (1,2), but is untested for use with human endothelial cells. The attachment of cells to surfaces is thought to be mediated by two serum components, fibronectin (FN) (3) and vitronectin (VN) (4). We have examined the attachment and spreading of human endothelial cells to Nafion surfaces, and the relative contribution of FN and VN in the adhesion of these cells on Nafion and on tissue culture polystyrene (TCP), using the method of selectively removing FN and VN from serum. This provides information on the role that these glycoproteins play in endothelial cell attachment, and the desirability of precoating Nafion with an attachment factor such as FN prior to exposure to human endothelial cells.

MATERIALS AND METHODS Nafion (Du Pont) substrates were prepared by solvent casting a solution of Nafion EW1100 (Solution Technology, Mendenhall, PA, USA) onto 22 mm tissue culture plastic wells at 60°C for 2 h. After sterilization by exposure to UV light for 2 h, the surfaces were equilibrated in serum free tissue culture medium at 37°C. Human umbilical artery endothelial (HUAE) cells were established according to routine methods and maintained in McCoys:Wissler medium (50:50, vol:vol)

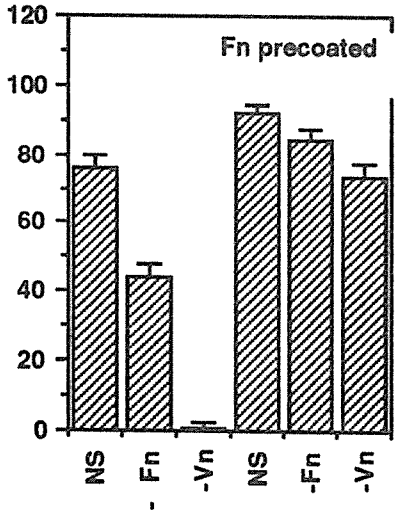
supplemented with 30% foetal bovine serum, fibroblast growth factor 40 $ngml^{-1}$ and endothelial cell growth supplement 60 $ugml^{-1}$. In other experiments the Nafion substrate was precoated with between 10-100 mg/ml^{-1} bovine plasma fibronectin, prior to seeding with cells. Serum to be used in the culture medium in some experiments was depleted of VN by chromatography on an anti-VN monoclonal antibody affinity column or depleted of FN by chromatography on a gelatin-Sepharose affinity column. Cell attachment and spreading was assessed by seeding approximately 10^5 cells per 22 mm well in 1 ml medium containing the appropriate serum preparation - normal serum, FN depleted serum or VN depleted serum at a concentration of 15%. Tissue culture plastic (TCP) was used as a control substrate. After 4 hours, 4 areas of each culture were examined by phase contrast microscopy, photographed and the proportion of spread cells (± standard error) calculated. Cells were judged to be spread when cell membrane ruffling was seen.

RESULTS The efficacy of procedures used to selectively remove FN and VN from serum was confirmed by enzyme linked immunosorbent assay (ELISA) using anti-FN and VN monoclonal antibodies. This demonstrated that levels were reduced to below 1.0% of normal serum values (results not shown). The attachment of HUAE cells on TCP was absolutely dependent upon serum VN serum (Fig. 1a). The removal of FN from serum decreased the attachment and spreading by only approximately 10% as compared to normal serum controls, indicating that serum FN was not as essential as serum VN. FN coated TCP provided an excellent substrate for HUAE cell attachment and spreading, and on this surface no significant differences were detected between cell cultures seeded in medium containing serum depleted of FN or VN, as compared with normal serum. Cell attachment and spreading on Nafion substrates was similar to TCP for all three medium preparations (Fig. 1b). In common with TCP, VN was shown to be an essential serum component for successful cell-Nafion interaction. In contrast to TCP, a greater dependence of cell attachment on Nafion upon serum FN was shown, as the number of cells attached and spread on Nafion was approximately 50% less than that on TCP when FN depleted serum was used. FN coating at 10 mg/ml^{-1} considerably increased the cell attachment and spreading on Nafion, however, maximum levels were achieved by seeding the cells on this surface in normal serum containing medium. Cells seeded in FN depleted and VN depleted sera attached and spread less well on FN coated Nafion compared to normal serum containing medium. This dependance on FN for human cells was in contrast to our previous report

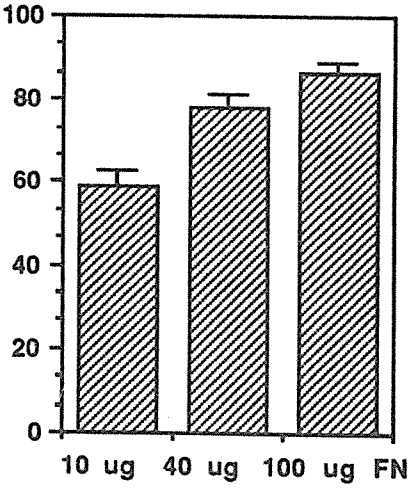
A. Attachment to TCP



B. Attachment to NAFION



C. Effect of Fn concentration on cell attachment to NAFION



(1) where we demonstrated that bovine aortic endothelial cells attached and grew on Nafion without a requirement for FN coating to givethe same cell response as that seen on TCP. To determine the optimum concentration of FN required to satisfactorily coat Nafion, three concentrations were assessed and the cell attachment then determined in VN depleted serum. Fig. 1c demonstrates that with an increase of the amount of FN up to 100 mg ml^{-1} an increase in cell attachment and spreading was observed.

DISCUSSION The logical design of biomaterials may be assisted by identification and understanding of the factors which govern specific aspects of the biological response to them. We have shown previously that Nafion provided a suitable substrate for the attachment and growth of bovine aortic endothelial cells (1). This present study demonstrates that Nafion is a suitable substrate for HUAE cells and comparable to TCP, and that coating Nafion with a biological attachment factor such as FN enhances human cell attachment and growth on Nafion. Furthermore we have shown that on uncoated TCP and Nafion, vitronectin is the major serum component responsible for the mediation of cell attachment and spreading. Coating both surfaces with FN precludes this requirement for serum VN, absolutely on TCP and partially in the case of Nafion (possibly depending on the concentration of FN used). This study not only highlights the similarity between Nafion and TCP as a cell substratum, but suggests that cells derived from different species (and possibly anatomical sites) may have different substrate requirements for attachment and growth.

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